Anti-PD1 17D8 VH

V segment: 3-33
D segment: unknown
J segment: JH4b

```
     Q   V   Q   L   V   E   S   G   G   D   V   V   Q   P   G   G   S   L
1    CAG GTG CAG CTG GTG GAG TCT GGG GGA GAC GTG GTC CAG CCT GGG GGG TCC CTG

                                                    CDR1
                                                    ~~~~~~~~~~~~~~~~~~
     R   L   S   C   A   A   S   G   V   A   F   S   N   Y   G   M   H   W
55   AGA CTC TCC TGT GCA GCG TCT GGA GTC GCC TTC AGT AAC TAT GGC ATG CAC TGG

                                                        CDR2
                                                        ~~~~~~~~~~~~~~~~~~
     V   R   Q   A   P   G   K   G   L   E   W   V   A   V   I   W   Y   D
109  GTC CGC CAG GCT CCC GGC AAG GGG CTG GAG TGG GTG GCA GTT ATC TGG TAT GAT

                    CDR2
     ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
     G   S   N   K   Y   Y   A   D   S   V   K   G   R   F   T   I   S   R
163  GGA AGT AAT AAA TAC TAT GCA GAC TCC GTG AAG GGC CGG TTC ACC ATC TCC AGA


     D   N   S   K   N   M   L   Y   L   Q   M   N   S   L   R   A   E   D
217  GAC AAT TCC AAG AAC ATG CTC TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                        CDR3
                                        ~~~~~~~~~~~~~~~~
     T   A   M   Y   Y   C   A   R   N   D   D   Y   W   G   Q   G   T   L
271  ACG GCT ATG TAT TAC TGT GCG AGG AAC GAT GAC TAC TGG GGC CAG GGA ACC CTG

                                            JH4b
                                            ---->

     V   T   V   S   S
325  GTC ACC GTC TCC TCA
```

Figure 1A

Anti-PD1 17D8 VK

V segment: L6
J segment: JK4

```
      E   I   V   L   T   Q   S   P   A   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                            ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   Y   L   A   W   Y
55    GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC TGG TAC

                                                                CDR2
                                                            ~~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   G   Q   A   P   R   L   I   I   Y   D   A   S   N   R
109   CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC ATC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      ~~~~~~~
      A   T   G   I   P   A   R   F   S   G   S   G   S   G   T   D   F   T
163   GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                                    CDR3
                                                                ~~~~~~~~
      L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

            CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~
      R   S   N   W   P   L   T   F   G   G   G   T   K   V   E   I   K
271   CGT AGC AAC TGG CCT CTC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA
```



Figure 1B

Anti-PD-1 2D3 VH

V segment: 3-33
D segment: 7-27
J segment: JH4b

```
    Q   V   Q   L   V   E   S   G   G   D   V   V   Q   P   G   R   S   L
1   CAG GTG CAG CTG GTG GAA TCT GGG GGA GAC GTG GTC CAG CCT GGG AGG TCC CTG

                                                    CDR1
                                                    ~~~~~~~~~~~~~~~~~~
    R   L   S   C   A   A   S   G   L   T   F   T   N   Y   G   F   H   W
55  AGA CTC TCC TGT GCA GCG TCT GGA TTA ACC TTC ACT AAC TAT GGC TTC CAC TGG

                                                        CDR2
                                                        ~~~~~~~~~~~~~~~~~~
    V   R   Q   A   P   G   K   G   L   E   W   V   A   V   I   W   Y   D
109 GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCT GTT ATA TGG TAT GAT

                    CDR2
    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
    G   S   K   K   Y   Y   A   D   S   V   K   G   R   F   T   I   S   R
163 GGA AGT AAG AAA TAT TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

    D   N   S   K   N   T   L   Y   L   Q   M   N   N   L   R   A   E   D
217 GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AAC CTG AGA GCC GAG GAC

                                        CDR3
                                        ~~~~~~~~~~~~~~~~
    T   A   V   Y   Y   C   A   T   G   D   D   Y   W   G   Q   G   T   L
271 ACG GCT GTG TAT TAC TGT GCG ACT GGG GAT GAC TAC TGG GGC CAG GGA ACC CTG

    V   T   V   S   S
325 GTC ACC GTC TCC TCA
```

Figure 2A

Anti-PD-1 2D3 VK

V segment: L6
J segment: JK4

```
      E   I   V   L   T   Q   S   P   A   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                            ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   Y   L   A   W   Y
55    GCC ACC CTG TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC TGG TAC

                                                            CDR2
                                                        ~~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   D   T   S   N   R
109   CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT ACA TCC AAC AGG

      CDR2
      ~~~~~~~
      A   T   G   I   P   A   R   F   S   G   S   G   S   G   T   D   F   T
163   GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                                    CDR3
                                                                ~~~~~~~~
      L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

              CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~
      R   S   N   W   P   L   T   F   G   G   G   T   K   V   E   I   K
271   CGT AGC AAC TGG CCG CTC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA
```

Figure 2B

Anti-PD-1 4H1 VH

V segment: 3-33
D segment: undetermined
J segment: JH4b

```
     Q   V   Y   L   V   E   S   G   G   G   V   V   Q   P   G   R   S   L
1    CAG GTG TAC TTG GTA GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                                        CDR1
                                                    ~~~~~~~~~~~~~~~~~~~
     R   L   S   C   A   A   S   G   F   T   F   S   N   Y   G   M   H   W
55   AGA CTC TCC TGT GCA GCG TCT GGA TTC ACC TTC AGT AAC TAT GGC ATG CAC TGG

                                                            CDR2
                                                    ~~~~~~~~~~~~~~~~~~~
     V   R   Q   A   P   G   K   G   L   E   W   V   A   L   I   W   Y   D
109  GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA CTT ATA TGG TAT GAT

                        CDR2
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
     G   S   N   K   Y   Y   A   D   S   V   K   G   R   F   T   I   S   R
163  GGA AGT AAT AAA TAC TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA

     D   N   S   K   N   T   L   Y   L   Q   M   T   S   L   R   V   E   D
217  GAC AAT TCC AAG AAC ACG CTG TAT CTG CAA ATG ACC AGT CTG AGA GTC GAG GAC

                                        CDR3
                                    ~~~~~~~~~~~~~~~~
     T   A   V   Y   Y   C   A   S   N   V   D   H   W   G   Q   G   T   L
271  ACG GCT GTG TAT TAT TGT GCG AGC AAC GTT GAC CAT TGG GGC CAG GGA ACC CTG

     V   T   V   S   S
325  GTC ACC GTC TCC TCA
```

Figure 3A

Anti-PD-1 4H1 VK

V segment: L6
J segment: JK1

```
      E   I   V   L   T   Q   S   P   A   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                                CDR1
                            ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   Y   L   A   W   Y
55    GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGT AGT TAC TTA GCC TGG TAC

                                                            CDR2
                                                        ~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   D   A   S   N   R
109   CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      ~~~~~~~
      A   T   G   I   P   A   R   F   S   G   S   G   S   G   T   D   F   T
163   GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                                CDR3
                                                            ~~~~~~~~
      L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

                CDR3
            ~~~~~~~~~~~~~~~~~~~~~~~~~~~
      S   S   N   W   P   R   T   F   G   Q   G   T   K   V   E   I   K
271   AGT AGC AAC TGG CCT CGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
```

Figure 3B

Anti-PD1 5C4 VH

V segment: 3-33
D segment: unknown
J segment: JH4b

```
      Q   V   Q   L   V   E   S   G   G   G   V   V   Q   P   G   R   S   L
1     CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                                        CDR1
                                                        ~~~~~~~~~~~~~~~~~~
      R   L   D   C   K   A   S   G   I   T   F   S   N   S   G   M   H   W
55    AGA CTC GAC TGT AAA GCG TCT GGA ATC ACC TTC AGT AAC TCT GGC ATG CAC TGG

                                                            CDR2
                                                            ~~~~~~~~~~~~~~~~~~
      V   R   Q   A   P   G   K   G   L   E   W   V   A   V   I   W   Y   D
109   GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTT ATT TGG TAT GAT

                        CDR2
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      G   S   K   R   Y   Y   A   D   S   V   K   G   R   F   T   I   S   R
163   GGA AGT AAA AGA TAC TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA


      D   N   S   K   N   T   L   F   L   Q   M   N   S   L   R   A   E   D
217   GAC AAT TCC AAG AAC ACG CTG TTT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                        CDR3
                                        ~~~~~~~~~~~~~~~~
      T   A   V   Y   Y   C   A   T   N   D   D   Y   W   G   Q   G   T   L
271   ACG GCT GTG TAT TAC TGT GCG ACA AAC GAC GAC TAC TGG GGC CAG GGA ACC CTG
                                    ┗━━━▶
                                        JH4b

      V   T   V   S   S
325   GTC ACC GTC TCC TCA
```

Figure 4A

Anti-PD1 5C4 VK

V segment: L6
J segment: JK1

```
      E   I   V   L   T   Q   S   P   A   T   L   S   L   S   P   G   E   R
1     GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                              CDR1
                              ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      A   T   L   S   C   R   A   S   Q   S   V   S   S   Y   L   A   W   Y
55    GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGT AGT TAC TTA GCC TGG TAC

                                                              CDR2
                                                              ~~~~~~~~~~~~~~~~~~~
      Q   Q   K   P   G   Q   A   P   R   L   L   I   Y   D   A   S   N   R
109   CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      ~~~~~~~
      A   T   G   I   P   A   R   F   S   G   S   G   S   G   T   D   F   T
163   GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                                      CDR3
                                                                      ~~~~~~~
      L   T   I   S   S   L   E   P   E   D   F   A   V   Y   Y   C   Q   Q
217   CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

                  CDR3
      ~~~~~~~~~~~~~~~~~~~~~~~~~~~~
      S   S   N   W   P   R   T   F   G   Q   G   T   K   V   E   I   K
271   AGT AGC AAC TGG CCT CGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
```

Figure 4B

Anti-PD-1 4A11 VH

V segment: 4-39
D segment: 3-9
J segment: JH4b

```
                Q   L   Q   L   Q   E   S   G   P   G   L   V   K   P   S   E   T   L
1       CAG CTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG

                                                                CDR1
                                                    ~~~~~~~~~~~~~~~~~~~~~~~~
                S   L   T   C   T   V   S   G   G   S   L   S   R   S   S   F   F   W
55      TCC CTC ACC TGC ACT GTC TCT GGT GGC TCC CTC AGC AGG AGT AGT TTC TTC TGG

                CDR1                                                        CDR2
                ~~~~                                                        ~~~~~~~~~~~
                G   W   I   R   Q   P   P   G   K   G   L   E   W   I   G   S   I   Y
109     GGC TGG ATC CGT CAG CCC CCA GGG AAG GGA CTG GAG TGG ATT GGG AGT ATC TAT

                        CDR2
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                Y   S   G   S   T   Y   Y   N   P   S   L   K   S   R   V   T   I   S
163     TAT AGT GGG AGC ACC TAC TAC AAC CCG TCC CTC AAG AGT CGA GTC ACC ATA TCC

                V   D   T   S   K   N   Q   F   S   L   K   L   S   S   V   T   A   A
217     GTA GAC ACG TCC AAG AAC CAG TTC TCC CTG AAG CTG AGC TCT GTG ACC GCC GCA

                                                        CDR3
                                        ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                D   T   A   V   Y   Y   C   V   R   D   Y   D   I   L   T   G   D   E
271     GAC ACG GCT GTG TAT TAC TGT GTG AGA GAT TAC GAT ATT TTG ACT GGC GAC GAG

                CDR3
                ~~~~~~~
                D   Y   W   G   Q   G   T   L   V   T   V   S   S
325     GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC GTG TCC TCA
```

Figure 5A

Anti-PD-1 4A11 VK

V segment: L15
J segment: JK1

```
                D   I   Q   M   T   Q   S   P   S   S   L   S   A   S   V   G   D   R
1       GAC ATC CAG ATG ACC CAG TCT CCA TCC TCA CTG TCT GCA TCT GTG GGA GAC AGA

                                    CDR1
                                    ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                V   S   I   T   C   R   A   S   Q   G   I   S   S   W   L   A   W   Y
55      GTC TCC ATC ACT TGT CGG GCG AGT CAG GGT ATT AGC AGC TGG TTA GCC TGG TAT

                                                                    CDR2
                                                                    ~~~~~~~~~~~~~~~~~~
                Q   Q   K   P   E   K   A   P   K   S   L   I   Y   A   A   S   N   L
109     CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA TCC AAT TTA

                CDR2
                ~~~~~~~
                R   S   G   V   P   S   R   F   S   G   S   G   S   G   T   D   F   T
163     CGA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT

                                                                            CDR3
                                                                            ~~~~~~~
                L   T   I   S   S   L   Q   P   E   D   F   A   T   Y   Y   C   Q   Q
217     CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT TAT TAC TGC CAA CAG

                        CDR3
                        ~~~~~~~~~~~~~~~~~~~~~~~~~~~
                Y   Y   S   Y   P   R   T   F   G   Q   G   T   K   V   E   I   K
271     TAT TAT AGT TAC CCT AGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
```

Figure 5B

Anti-PD-1 7D3 VH

V segment: 3-33
D segment: 7-27
J segment: JH4b

```
                Q   V   Q   L   V   E   S   G   G   G   V   V   Q   P   G   R   S   L
1       CAG GTG CAG CTG GTG GAG TCT GGG GGA GGC GTG GTC CAG CCT GGG AGG TCC CTG

                                                                CDR1
                                                        ~~~~~~~~~~~~~~~~~~
                R   L   S   C   T   T   S   G   I   T   F   S   S   Y   G   F   H   W
55      AGA CTC TCC TGT ACA ACG TCT GGA ATC ACC TTC AGT AGC TAT GGC TTT CAC TGG

                                                            CDR2
                                                        ~~~~~~~~~~~~~~~~~~
                V   R   Q   A   P   G   K   G   L   E   W   V   A   V   I   W   Y   D
109     GTC CGC CAG GCT CCA GGC AAG GGG CTG GAG TGG GTG GCA GTG ATA TGG TAT GAT

                        CDR2
        ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                G   S   K   K   Y   Y   A   D   S   V   K   G   R   F   T   L   S   R
163     GGA AGT AAA AAA TAC TAT GCA GAC TCC GTG AAG GGC CGA TTC ACC CTC TCC AGA

                D   D   S   K   N   T   L   Y   L   Q   M   N   S   L   R   A   E   D
217     GAC GAT TCC AAG AAC ACG CTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC

                                        CDR3
                                ~~~~~~~~~~~~~~~~~
                T   A   V   Y   Y   C   V   T   G   D   D   Y   W   G   Q   G   T   L
271     ACG GCT GTG TAT TAC TGT GTT ACT GGG GAT GAC TAC TGG GGC CAG GGA ACC CTG

                V   T   V   S   S
325     GTC ACC GTC TCC TCA
```

Figure 6A

Anti-PD-1 7D3 VK

V segment: L6
J segment: JK4

```
1     E  I  V  L  T  Q  S  P  A  T  L  S  L  S  P  G  E  R
      GAA ATT GTG TTG ACA CAG TCT CCA GCC ACC CTG TCT TTG TCT CCA GGG GAA AGA

                        CDR1
                        ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
55    A  T  L  S  C  R  A  S  Q  S  V  S  S  Y  L  A  W  Y
      GCC ACC CTC TCC TGC AGG GCC AGT CAG AGT GTT AGC AGC TAC TTA GCC TGG TAC

                                                   CDR2
                                                   ~~~~~~~~~~~~~~~~~~~~
109   Q  Q  K  P  G  Q  A  P  R  L  L  I  Y  D  A  S  N  R
      CAA CAG AAA CCT GGC CAG GCT CCC AGG CTC CTC ATC TAT GAT GCA TCC AAC AGG

      CDR2
      ~~~~~~~
163   A  T  G  I  P  A  R  F  S  G  S  G  S  G  T  D  F  T
      GCC ACT GGC ATC CCA GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACT

                                                         CDR3
                                                         ~~~~~~~
217   L  T  I  S  S  L  E  P  E  D  F  A  V  Y  Y  C  Q  Q
      CTC ACC ATC AGC AGC CTA GAG CCT GAA GAT TTT GCA GTT TAT TAC TGT CAG CAG

            CDR3
            ~~~~~~~~~~~~~~~~~~~~~~~~~~~
271   R  S  N  W  P  L  T  F  G  G  G  T  K  V  E  I  K
      CGT AGC AAC TGG CCT CTC ACT TTC GGC GGA GGG ACC AAG GTG GAG ATC AAA
```

Figure 6B

Anti-PD-1 5F4 VH

V segment: 4-39
D segment: 3-9
J segment: JH4b

```
                Q   L   Q   L   Q   E   S   G   P   G   L   V   K   P   S   E   T   L
1       CAG CTG CAG CTG CAG GAG TCG GGC CCA GGA CTG GTG AAG CCT TCG GAG ACC CTG

                                                                CDR1
                                                        ~~~~~~~~~~~~~~~~~~~~~~
                S   L   T   C   S   V   S   G   G   S   L   S   R   S   S   Y   F   W
55      TCC CTC ACC TGC TCT GTC TCT GGT GGC TCC CTC AGC AGG AGT AGT TAC TTC TGG

        CDR1                                                            CDR2
        ~~~                                                             ~~~~~~~~~~
                G   W   I   R   Q   P   P   G   K   G   L   E   W   I   A   S   I   F
109     GGC TGG ATC CGC CAG CCC CCA GGG AAG GGG CTG GAG TGG ATT GCG AGT ATC TTT

                        CDR2
        ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                Y   S   G   E   T   Y   F   N   P   S   L   K   S   R   V   T   I   S
163     TAT AGT GGG GAA ACC TAC TTC AAT CCG TCC CTC AAG AGT CGA GTC ACC ATA TCC


                V   D   T   S   R   N   Q   F   S   L   K   L   S   S   V   T   A   A
217     GTA GAC ACG TCC AGG AAC CAG TTC TCC CTG AAG CTG AGC TCT GTG ACC GCC GCA

                                                        CDR3
                                                ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                D   T   A   V   Y   Y   C   A   R   D   Y   D   I   L   T   G   D   E
271     GAC ACG GCT GTG TAT TAC TGT GCG AGA GAT TAC GAT ATT TTG ACT GGC GAC GAG

        CDR3
        ~~~~~~~~
                D   Y   W   G   Q   G   T   L   V   T   V   S   S
325     GAC TAC TGG GGC CAG GGA ACC CTG GTC ACC GTC TCC TCA
```

Figure 7A

Anti-PD-1 5F4 VK

V segment: L15
J segment: JK1

```
                D   I   Q   M   T   Q   S   P   S   S   L   S   A   S   V   G   D   R
1       GAC ATC CAG ATG ACC CAG TCT CCA TCC TCA CTG TCT GCA TCT GTA GGA GAC AGA

                                    CDR1
                            ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
                V   T   I   T   C   R   A   S   Q   G   I   S   S   W   L   A   W   Y
55      GTC ACC ATC ACT TGT CGG GCG AGT CAG GGT ATT AGC AGC TGG TTA GCC TGG TAT

                                                                CDR2
                                                        ~~~~~~~~~~~~~~~~~~~~
                Q   Q   K   P   E   K   A   P   K   S   L   I   Y   A   A   S   S   L
109     CAG CAG AAA CCA GAG AAA GCC CCT AAG TCC CTG ATC TAT GCT GCA TCC AGT TTG

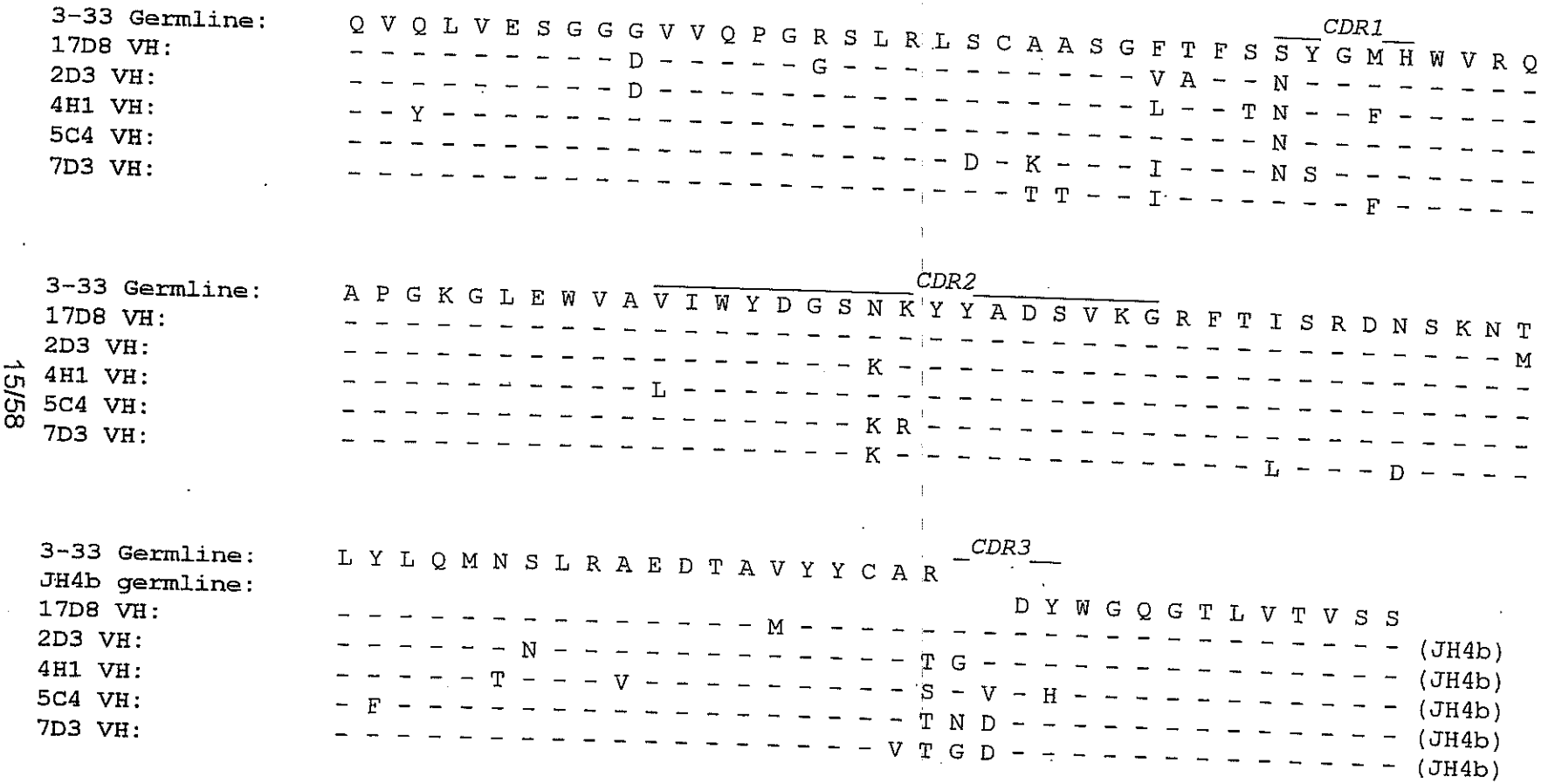
                CDR2
                ~~~~~~~
                Q   S   G   V   P   S   R   F   S   G   S   G   S   G   T   D   F   T
163     CAA AGT GGG GTC CCA TCA AGG TTC AGC GGC AGT GGA TCT GGG ACA GAT TTC ACT

                                                                        CDR3
                                                                        ~~~~~~~
                L   T   I   S   S   L   Q   P   E   D   F   A   T   Y   Y   C   Q   Q
217     CTC ACC ATC AGC AGC CTG CAG CCT GAA GAT TTT GCA ACT TAT TAC TGC CAA CAG

                        CDR3
                ~~~~~~~~~~~~~~~~~~~~~~~~~~~
                Y   Y   S   Y   P   R   T   F   G   Q   G   T   K   V   E   I   K
271     TAT TAT AGT TAC CCT AGG ACG TTC GGC CAA GGG ACC AAG GTG GAA ATC AAA
```

Figure 7B

Anti-PD1 17D8, 2D3, 4H1, 5C4 and 7D3 VH region


3-33 Germline: Q V Q L V E S G G G V V Q P G R S L R L S C A A S G F T F S S Y G M H W V R Q
CDR1
17D8 VH: - - - - - - - - - D - - - - - G - - - - - - - - - - V A - - N - - - - - - - -
2D3 VH: - - - - - - - - - D - - - - - - - - - - - - - - - - L - - T N - - F - - - - -
4H1 VH: - - Y - N - - - - - - -
5C4 VH: - D - K - - - I - - - N S - - - - - - -
7D3 VH: - T T - - I - - - - - - F - - - - -
3-33 Germline: A P G K G L E W V A V I W Y D G S N K Y Y A D S V K G R F T I S R D N S K N T
CDR2
17D8 VH: - - - - - - - - - - - - - - - - - - -

Anti-PD-1 17D8, 2D3 and 7D3 VK Region

```
                                                
```

Anti-PD-1 4H1 and 5C4 VK Region

```
                                                
```

Anti-PD-1 4A11 and 5F4 VH regions

```
                                                
```

Anti-PD-1 4A11 and 5F4 VK region

```
                                                                                                                CDR1
L15 germline:  D I Q M T Q S P S S L S A S V G D R V T I T C R A S Q G I S S
4A11 VK:       - - - - - - - - - - - - - - - - - - - - S - - - - - - - - - -
5F4 VK1:       - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -

                                                                CDR2
L15 germline:  W L A W Y Q Q K P E K A P K S L I Y A A S S L Q S G V P S R F
4A11 VK:       - - - - - - - - - - - - - - - - - - - - - - N - R - - - - - -
5F4 VK1:       - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -

                                                                        CDR3
L15 germline:  S G S G S G T D F T L T I S S L Q P E D F A T Y Y C Q Q Y N S
4A11 VK:       - - - - - - - - - - - - - - - - - - - - - - - - - - - - - Y -
5F4 VK1:       - - - - - - - - - - - - - - - - - - - - - - - - - - - - - Y -

L15 germline:  Y P
JK1 germline:      T F G Q G T K V E I K
4A11 VK:       - - R - - - - - - - - - (JK1)
5F4 VK1:       - - R - - - - - - - - - (JK1)
```

Figure 12

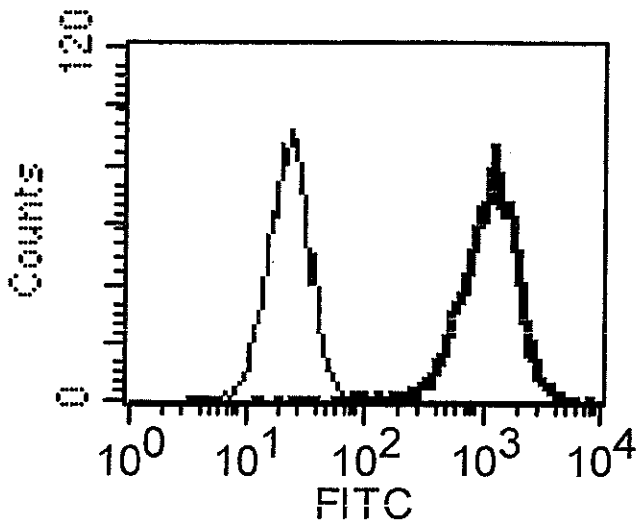


Figure 13A

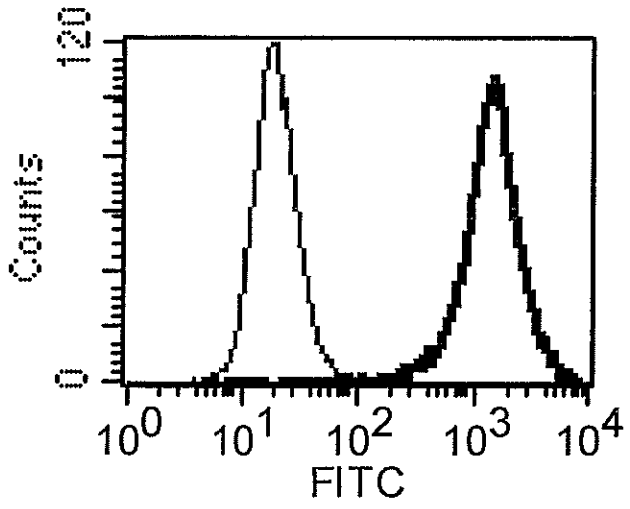


Figure 13B

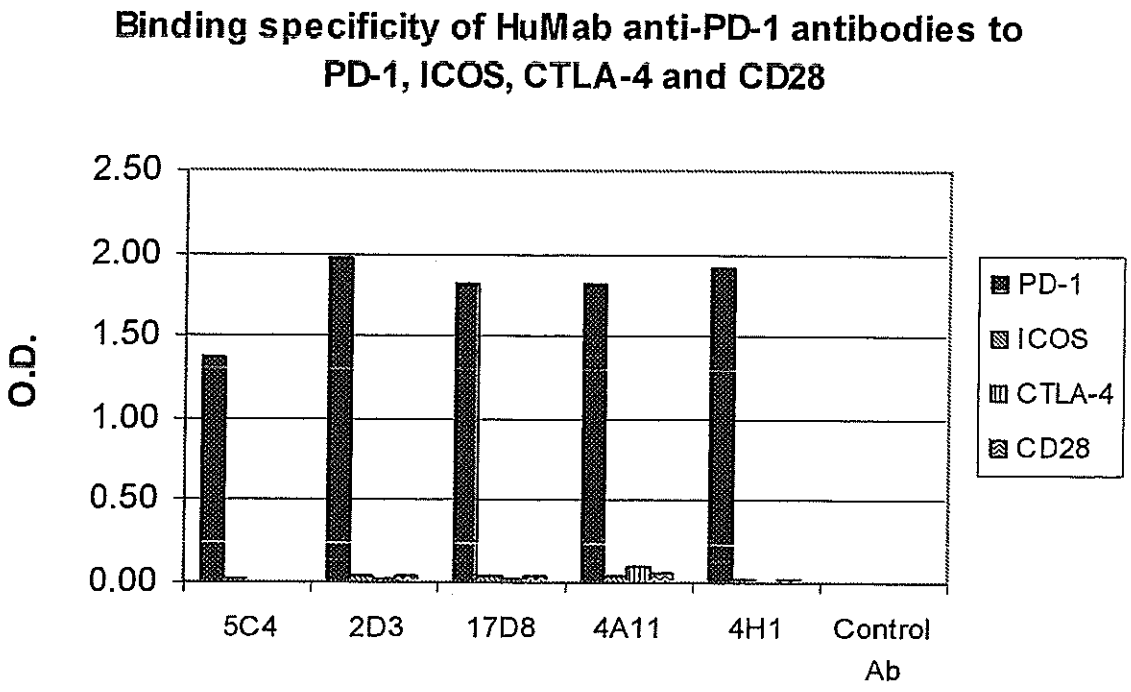

Binding specificity of HuMab anti-PD-1 antibodies to PD-1, ICOS, CTLA-4 and CD28
O.D.
2.50
2.00
1.50
1.00
0.50
0.00
5C4
2D3
17D8
4A11
4H1
Control Ab
PD-1
ICOS
CTLA-4
CD28

Figure 14

Binding of HuMab anti-hPD-1 Abs to activated human T cells

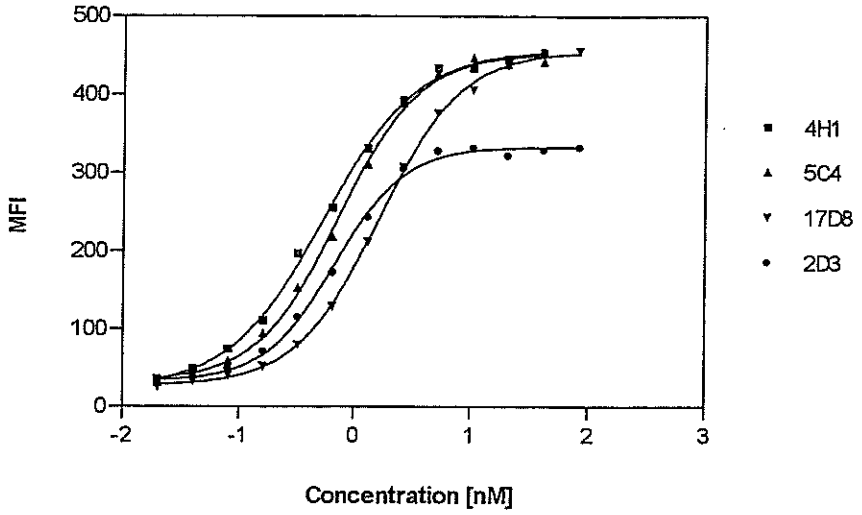


Figure 15A

Binding of HuMab anti-hPD-1 Abs to activated cynomolgous monkey PBMC

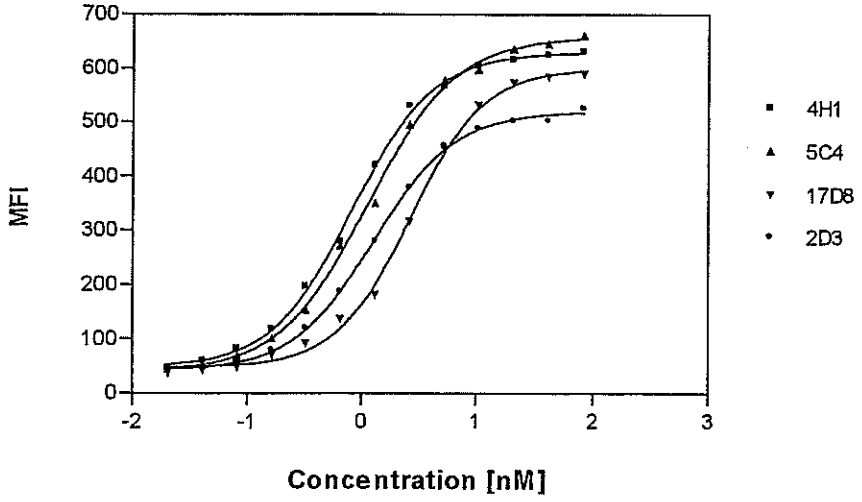


Figure 15B

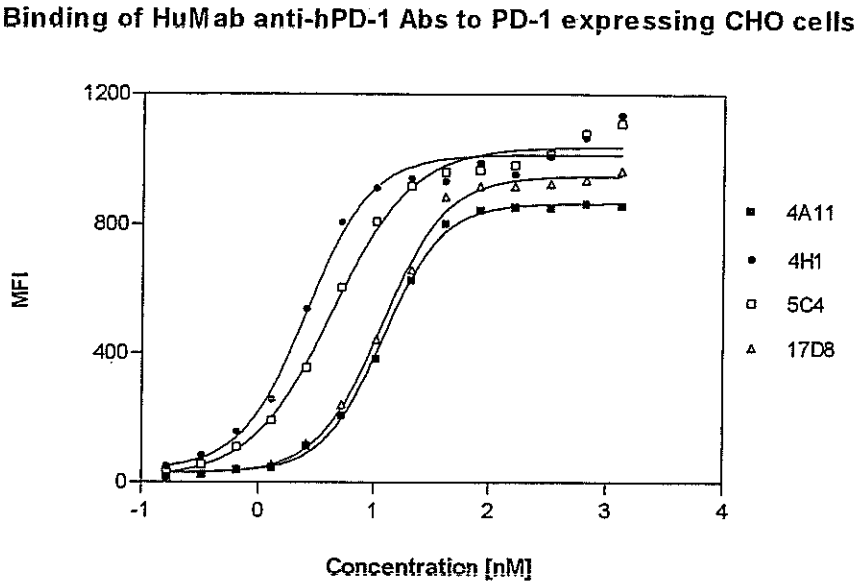

Binding of HuMab anti-hPD-1 Abs to PD-1 expressing CHO cells
MFI
1200
800
400
0
-1
0
1
2
3
4
Concentration [nM]
4A11
4H1
5C4
17D8

Figure 15C

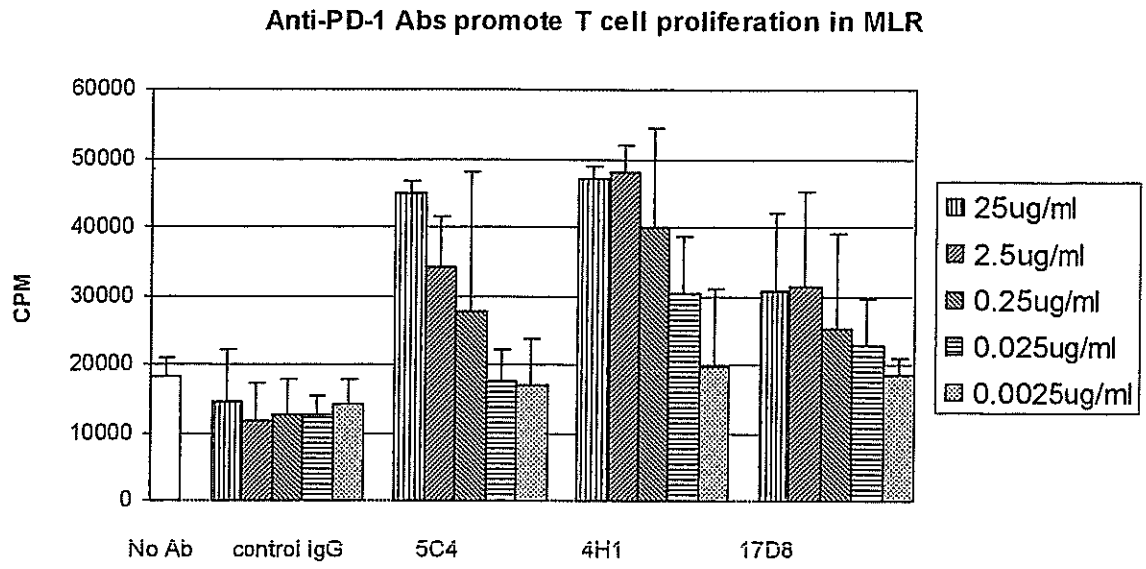


Figure 16A

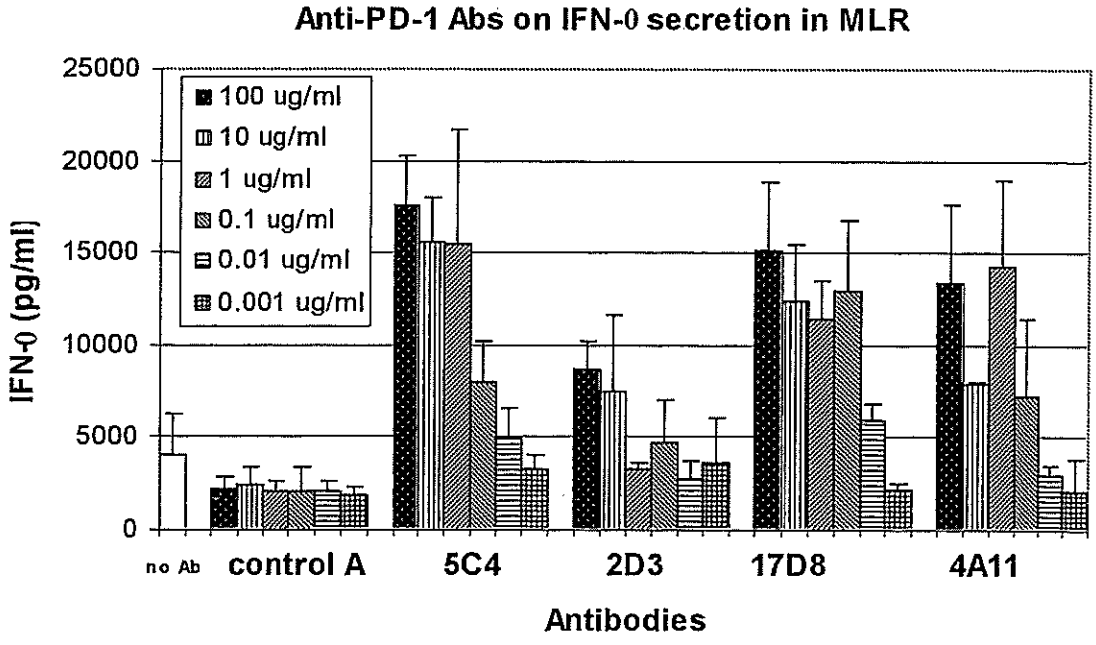


Figure 16B

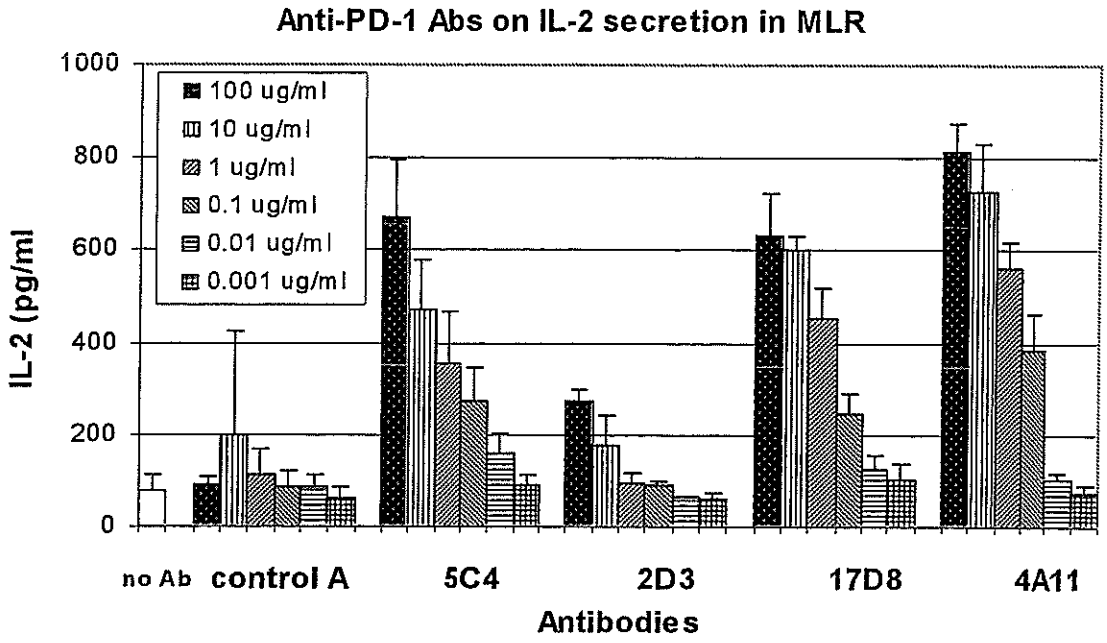

Anti-PD-1 Abs on IL-2 secretion in MLR
1000
800
600
400
200
0
IL-2 (pg/ml
100 ug/ml
10 ug/ml
1 ug/ml
0.1 ug/ml
0.01 ug/ml
0.001 ug/ml
no Ab
control A
5C4
2D3
17D8
4A11
Antibodies

Figure 16C

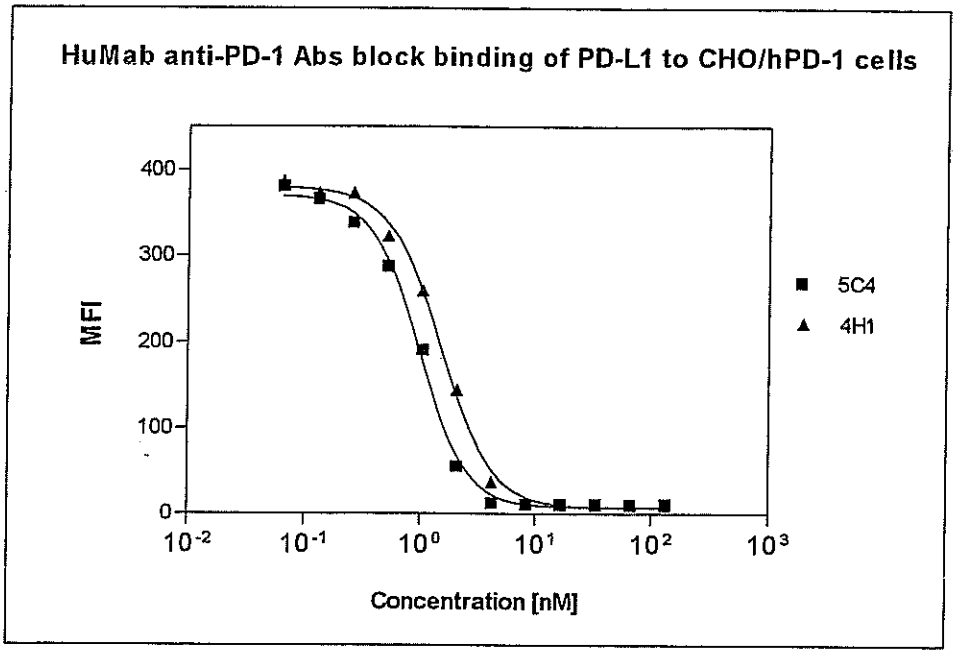


Figure 17A

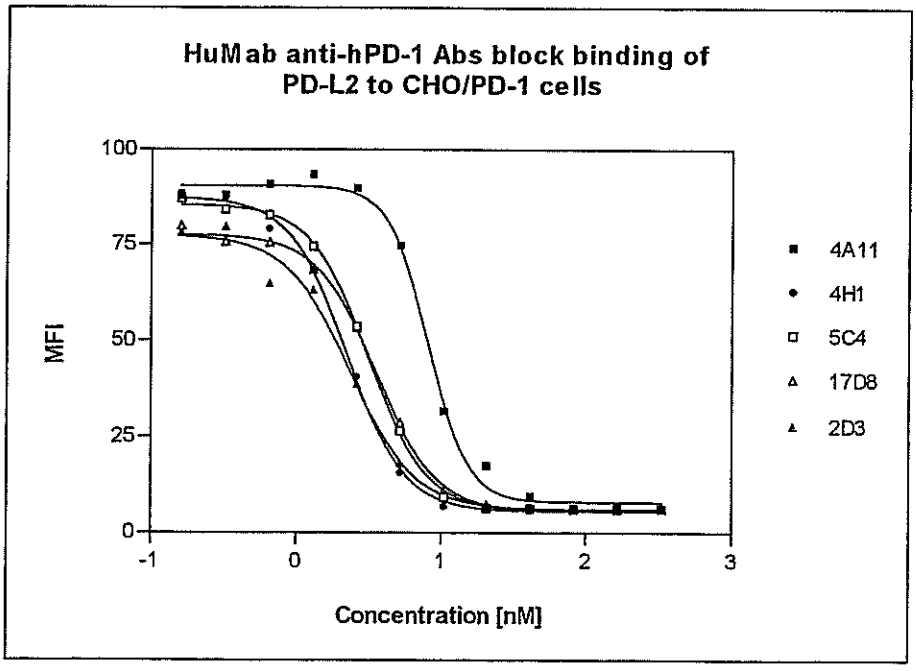


Figure 17B

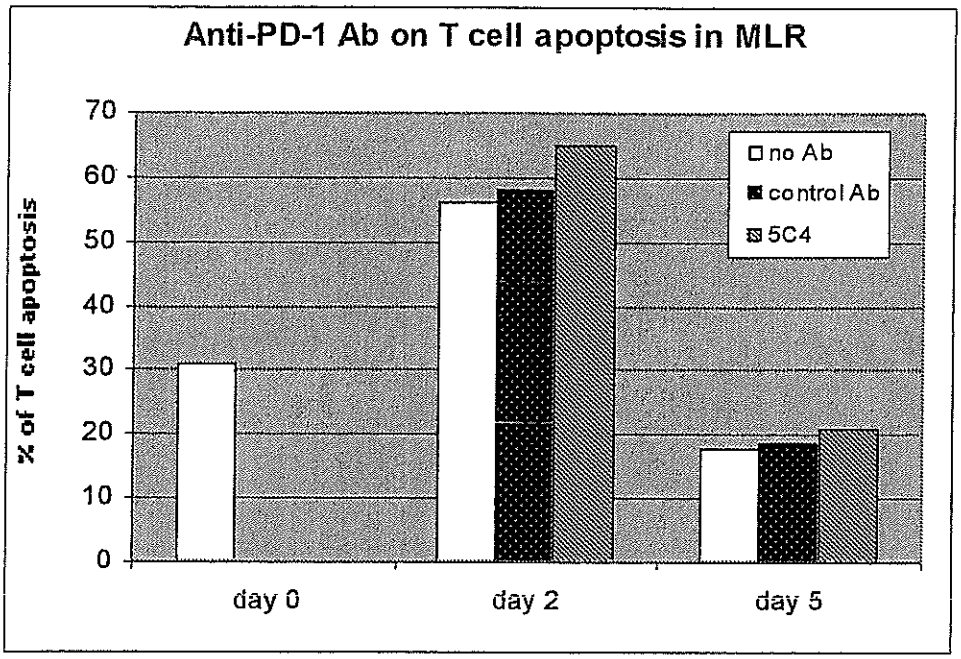


Figure 18

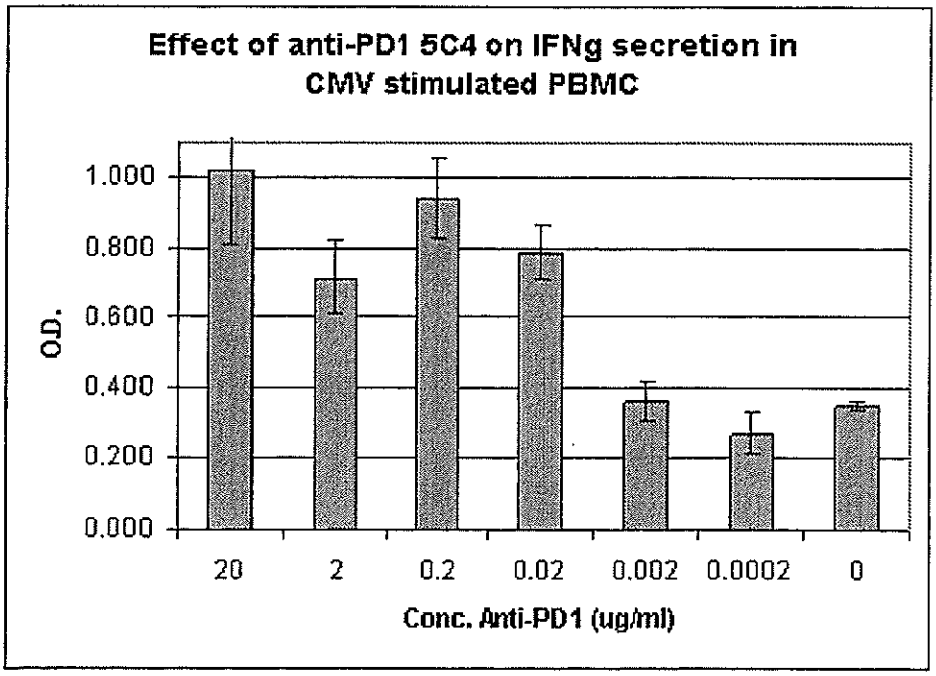


Figure 19

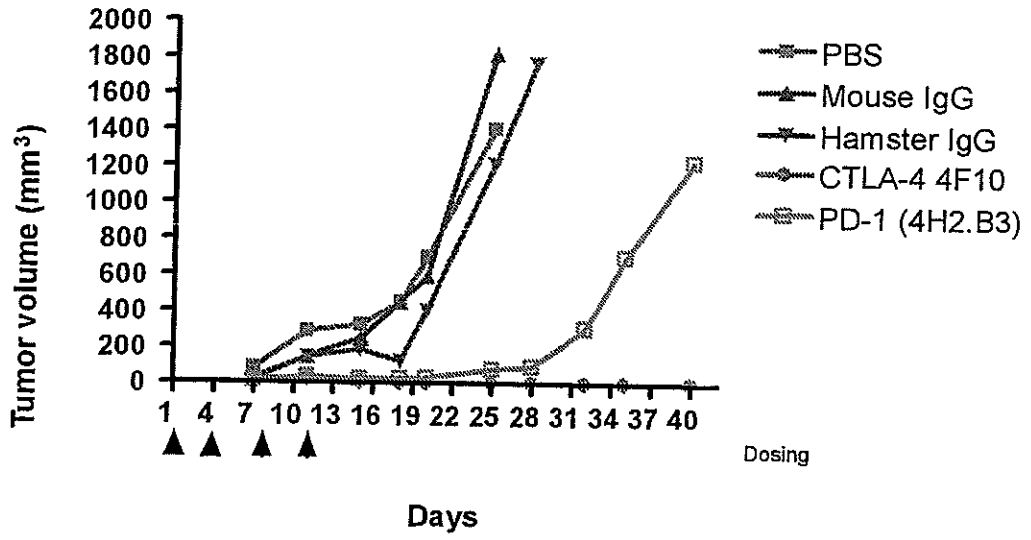

Tumor volume (mm³)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
1 4 7 10 13 16 19 22 25 28 31 34 37 40
Dosing
Days
PBS
Mouse IgG
Hamster IgG
CTLA-4 4F10
PD-1 (4H2.B3)

Figure 20

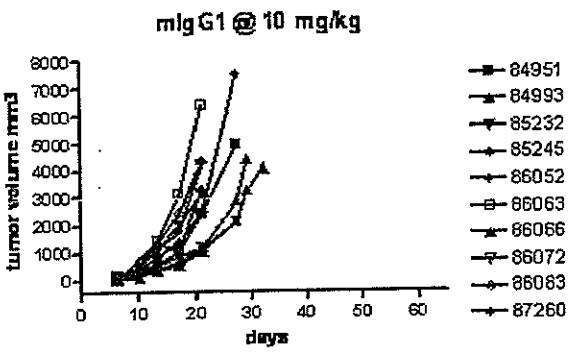


Figure 21A

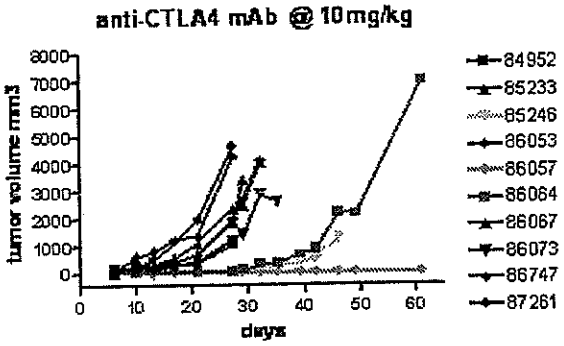


Figure 21B

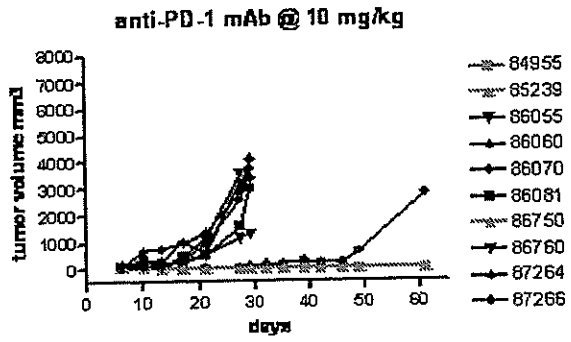


Figure 21C

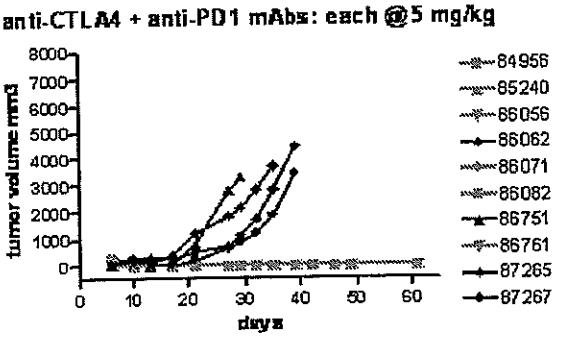


Figure 21D

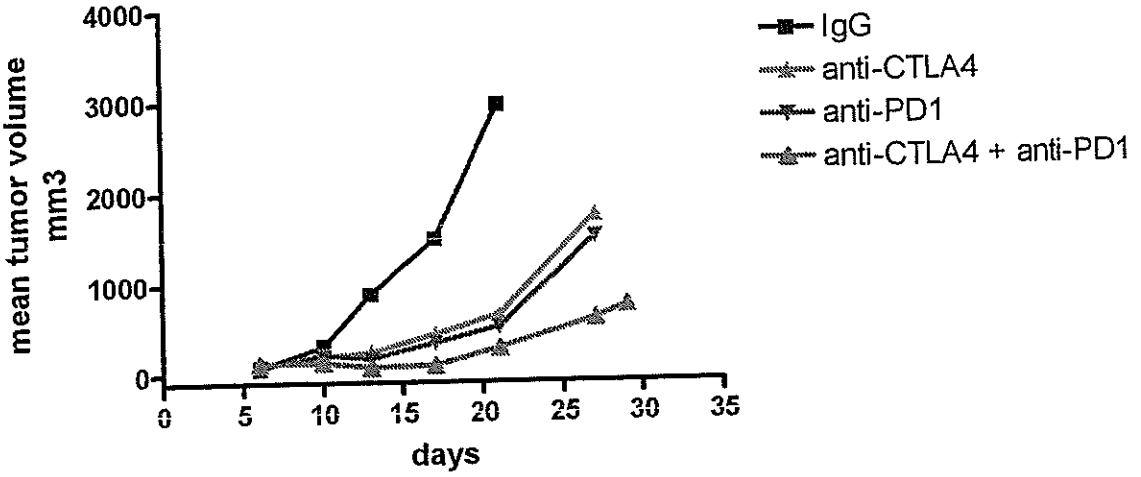


Figure 22

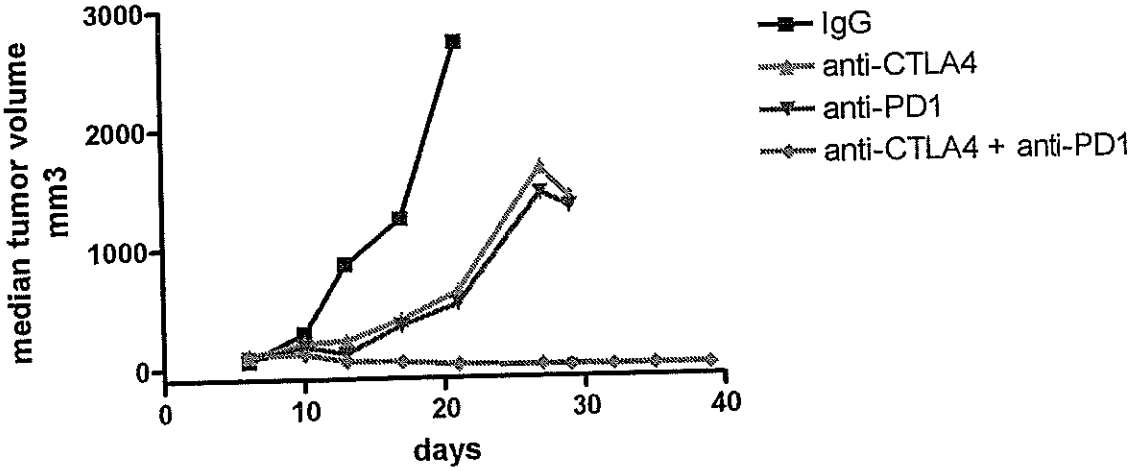


Figure 23

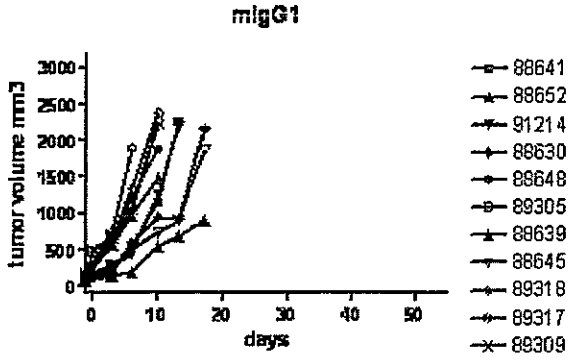


Figure 24A

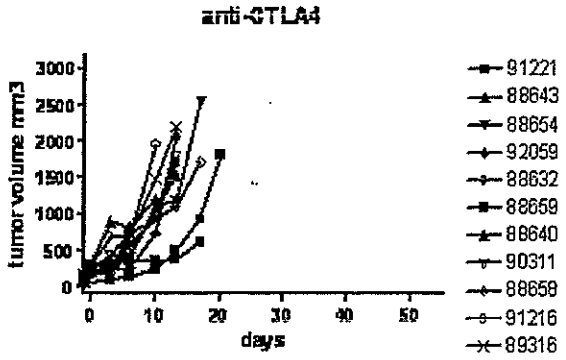


Figure 24B

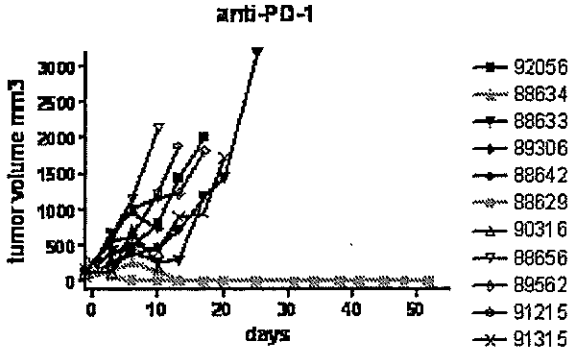


Figure 24C

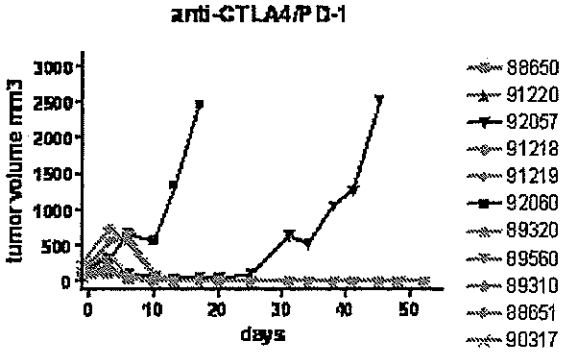


Figure 24D

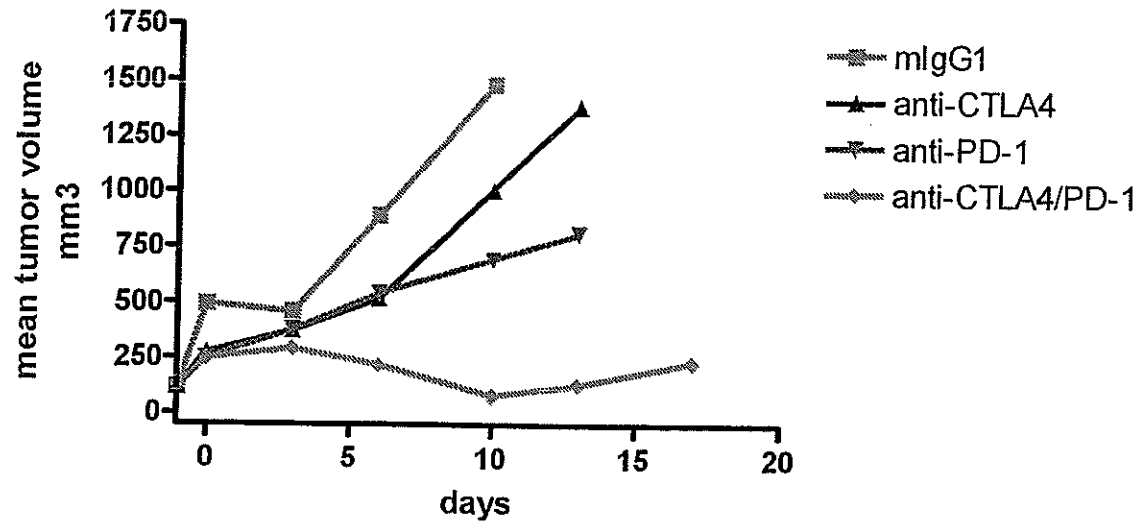


Figure 25

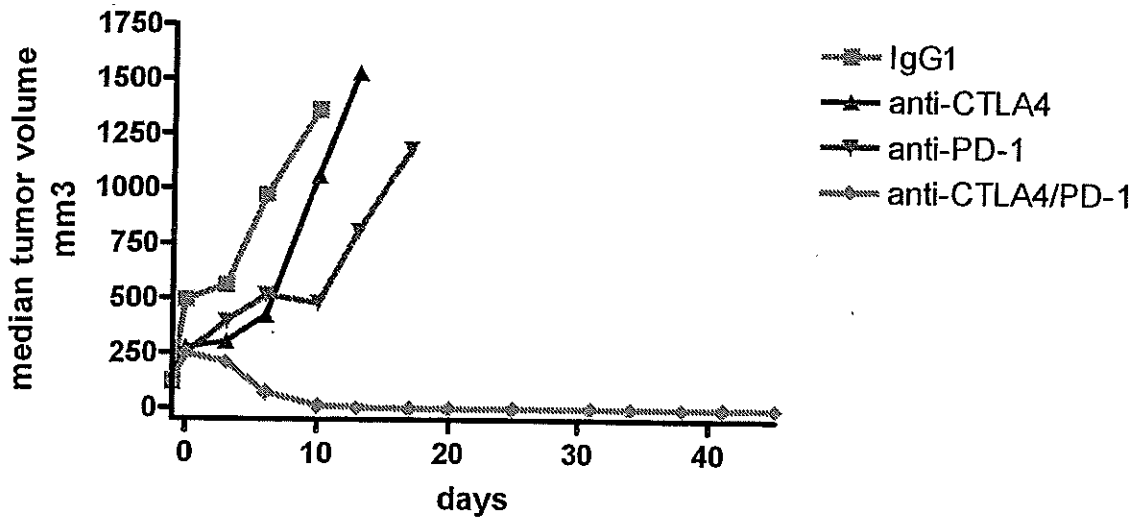


Figure 26

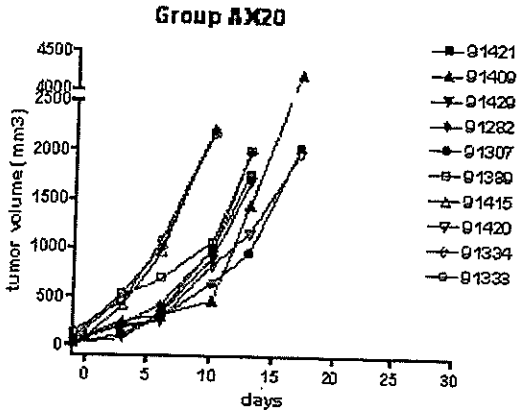


Figure 27A

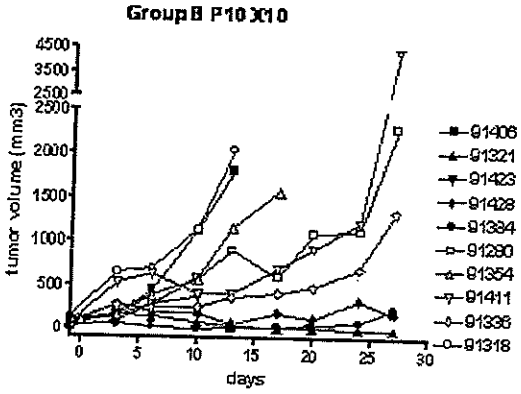


Figure 27B

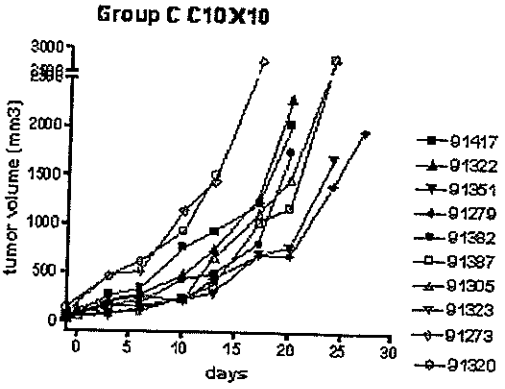


Figure 27C

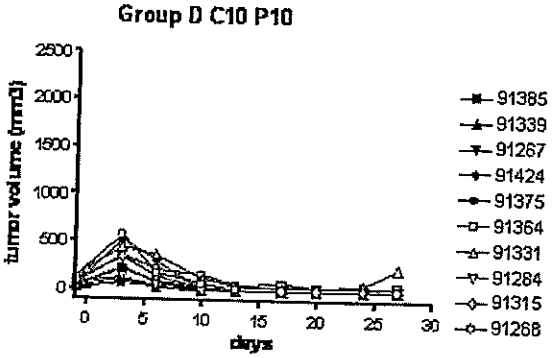


Figure 27D

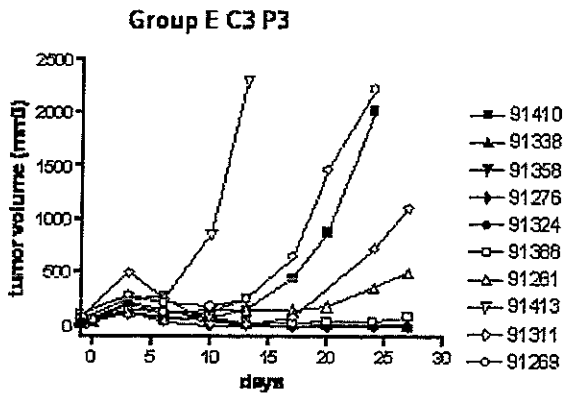


Figure 27E

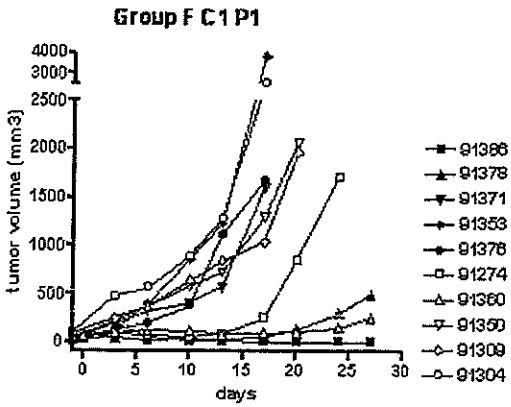


Figure 27F

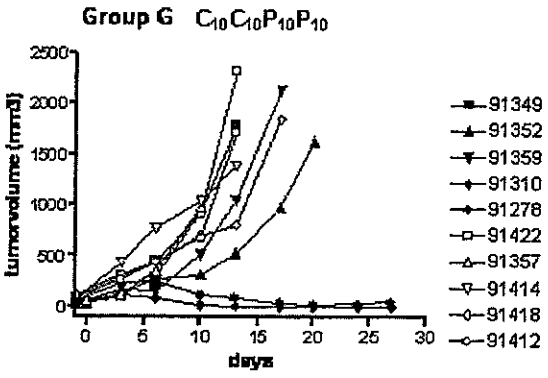


Figure 27G

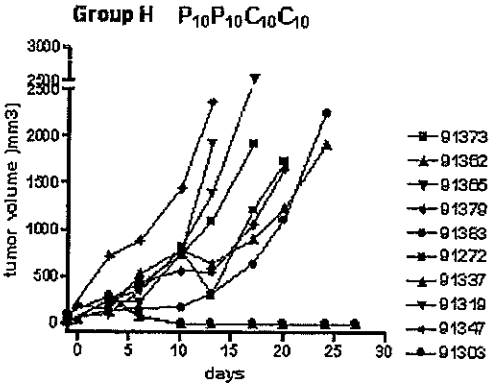


Figure 27H

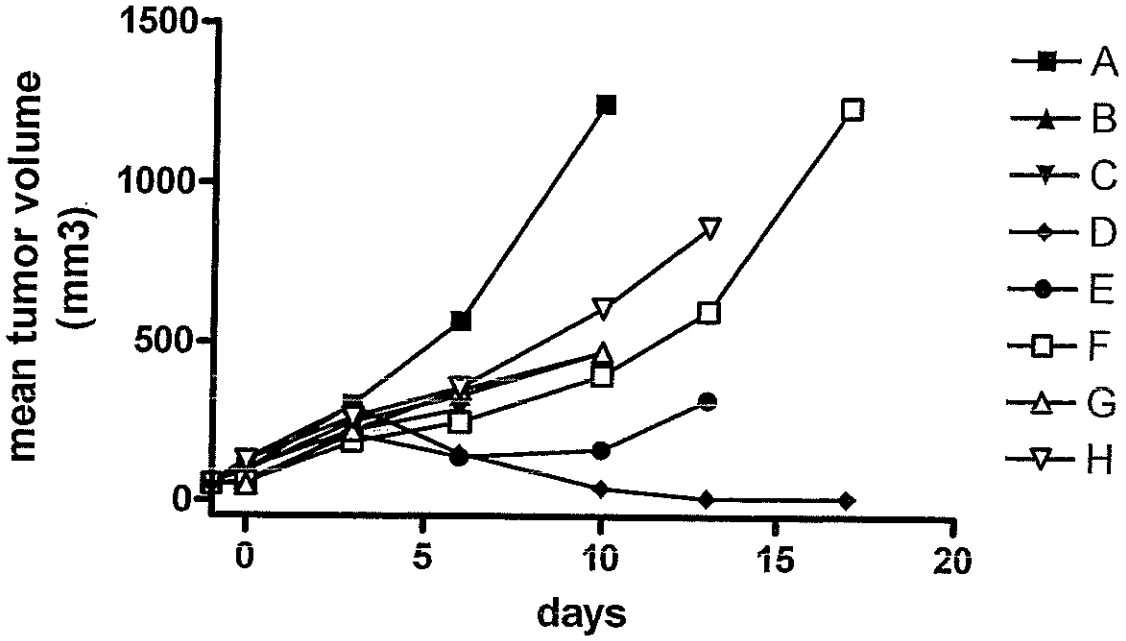


Figure 28

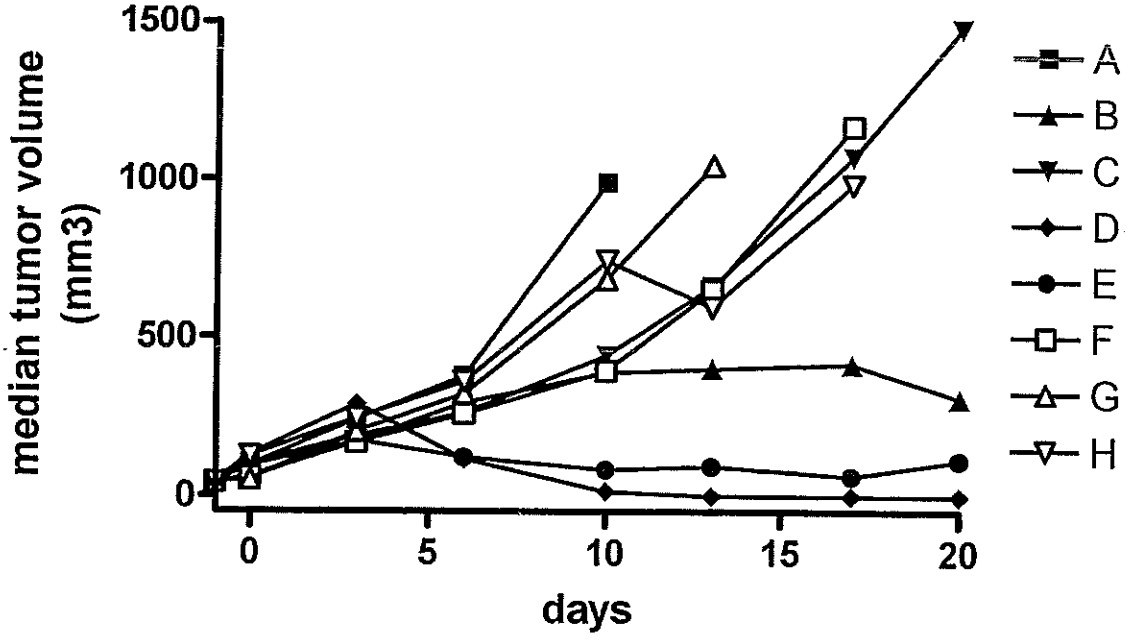


Figure 29

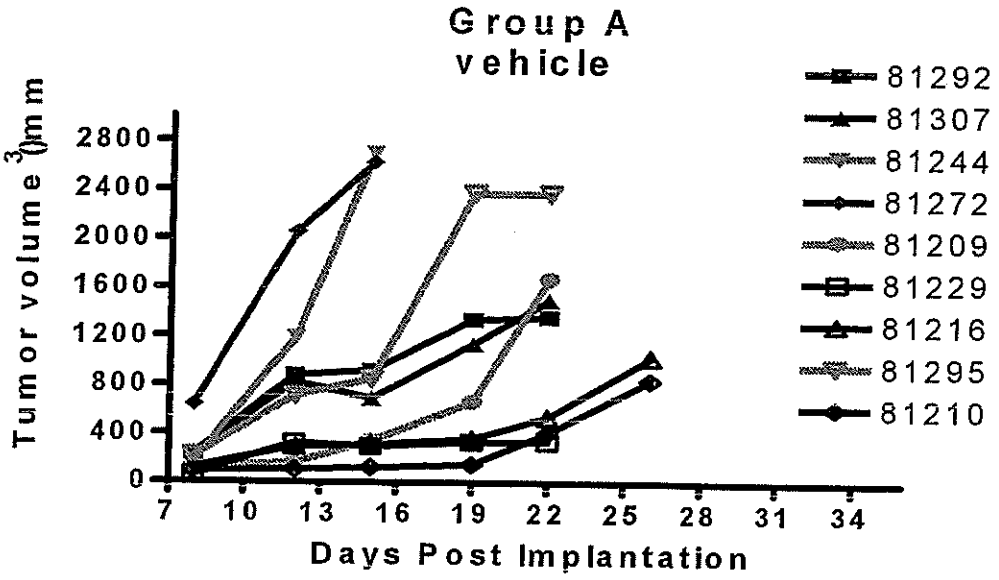


Figure 30A

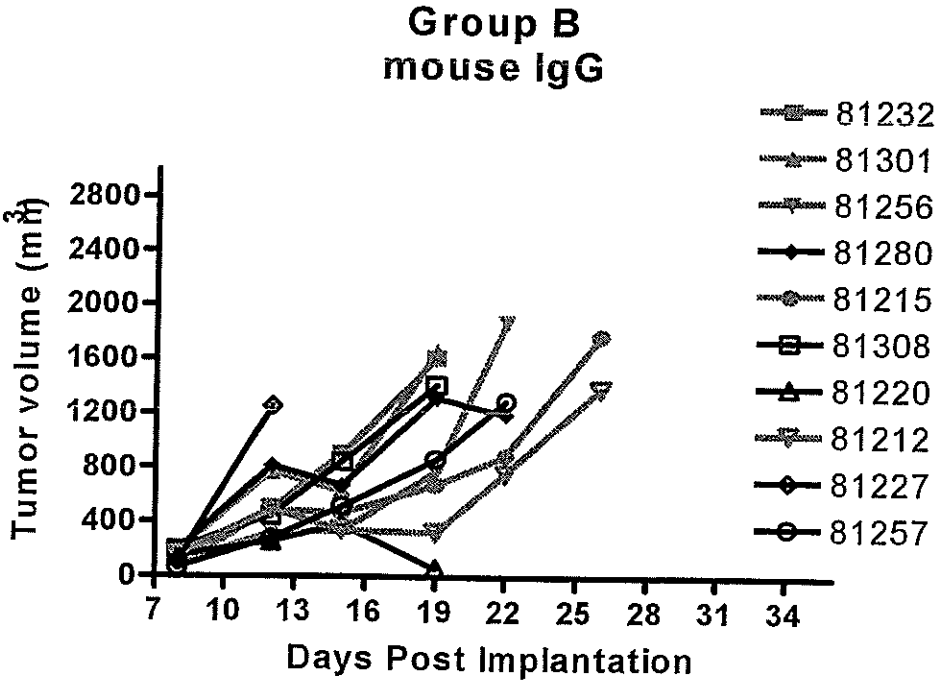


Figure 30B

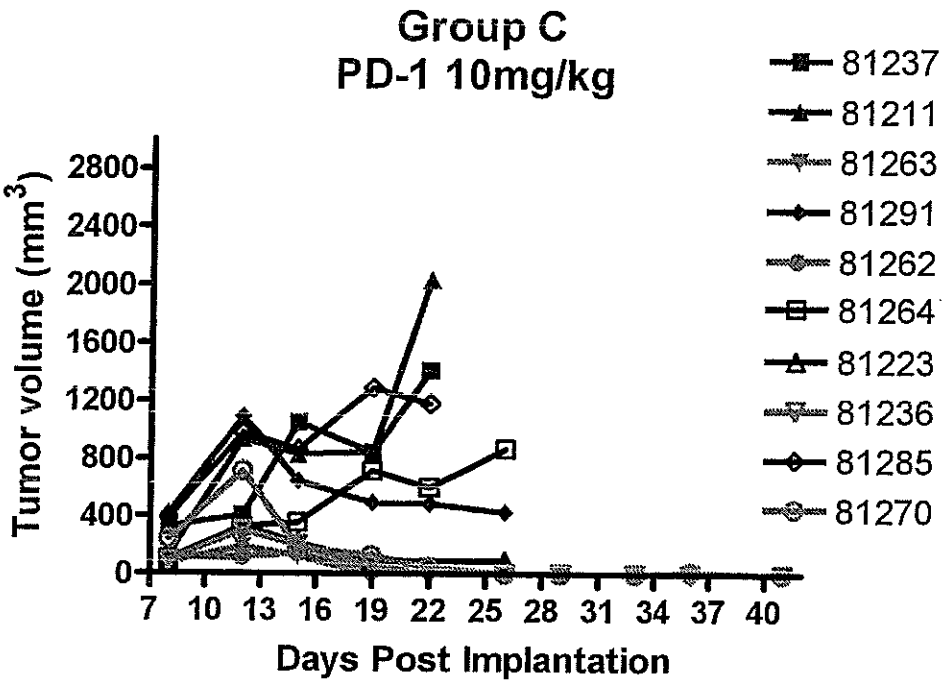


Figure 30C

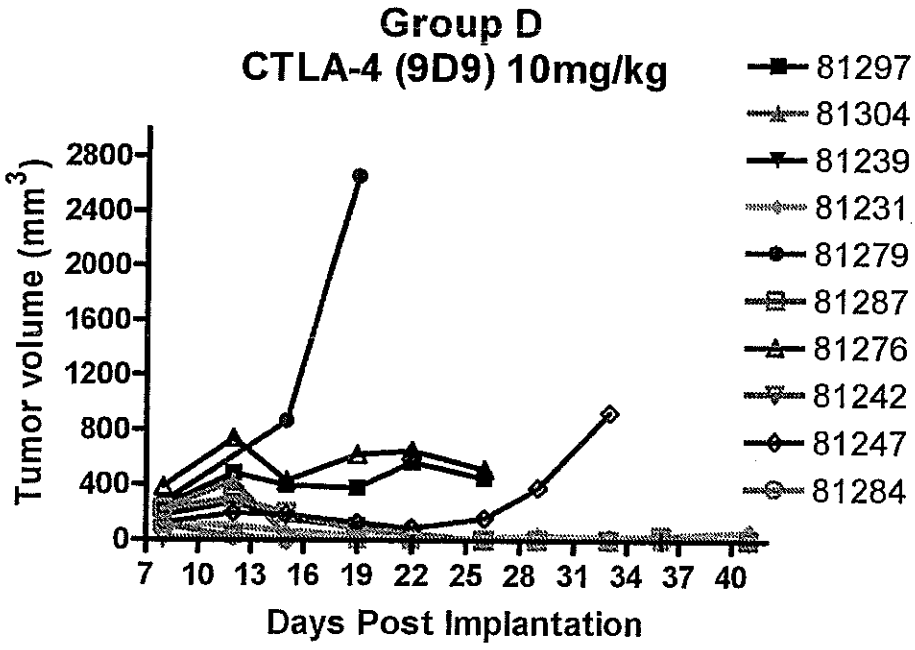


Figure 30D

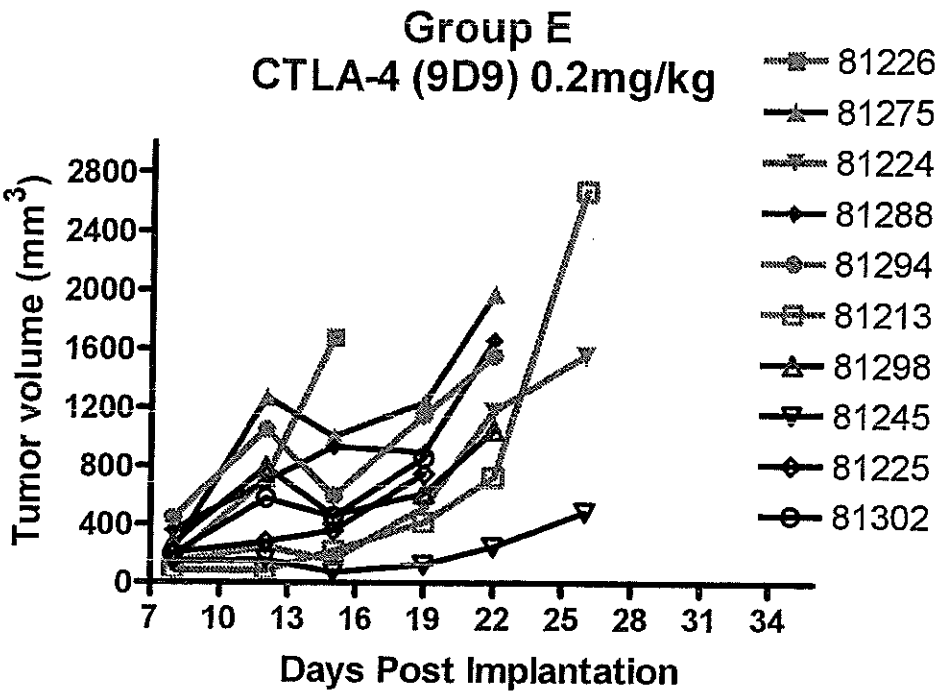


Figure 30E

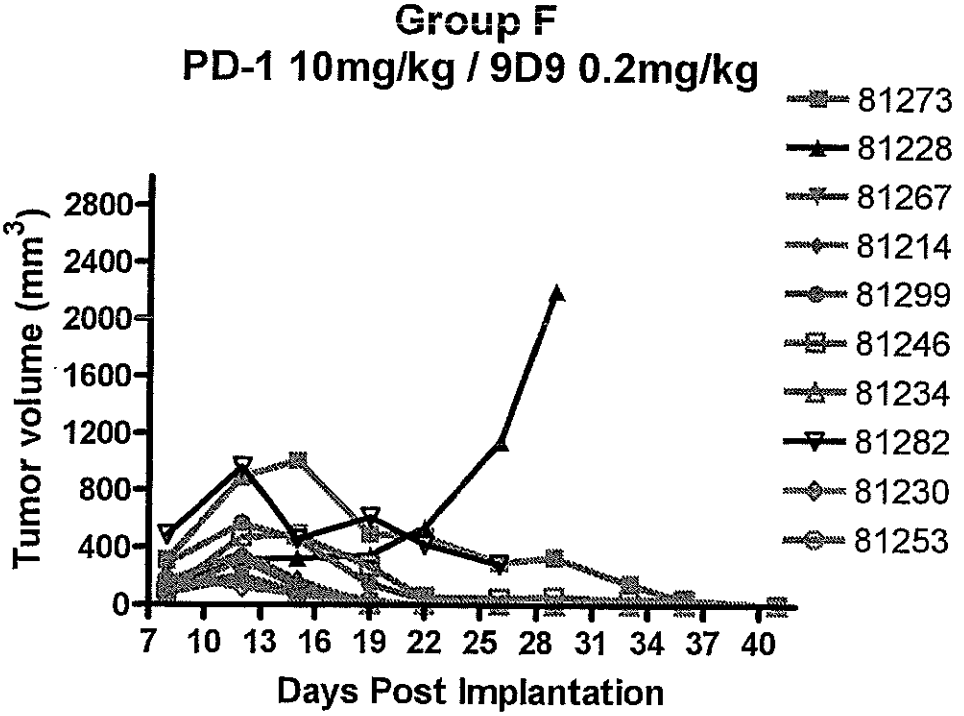


Figure 30F

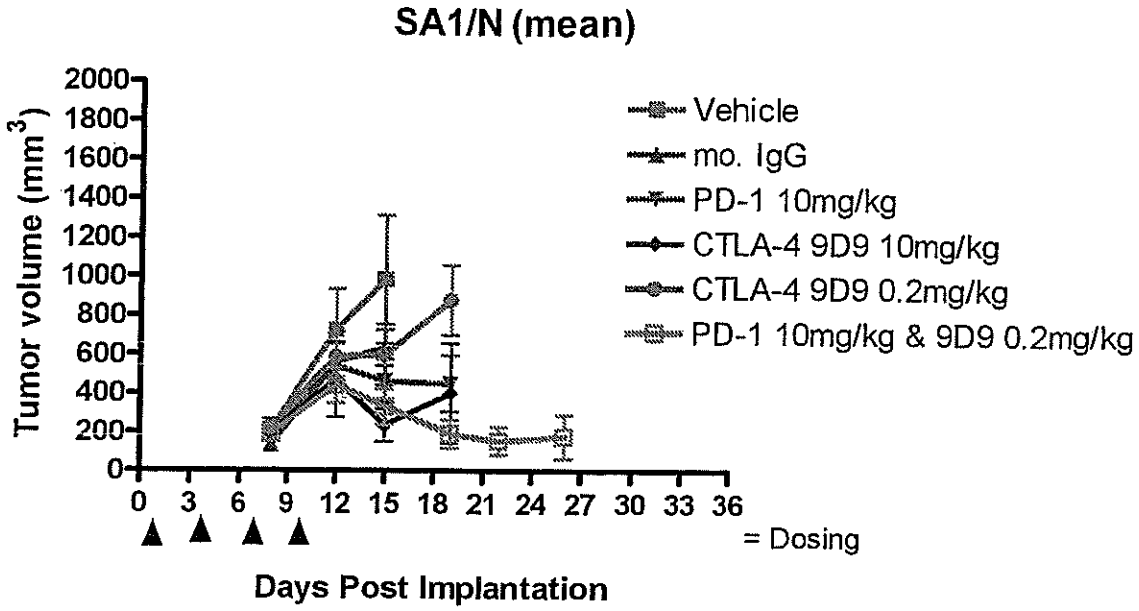


Figure 31

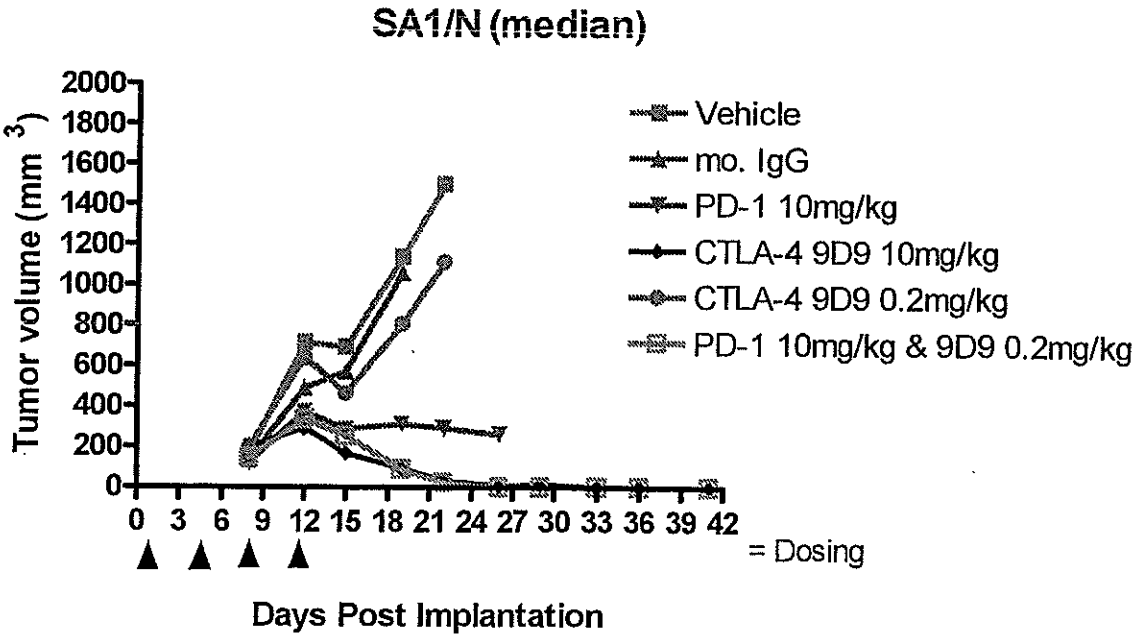


Figure 32

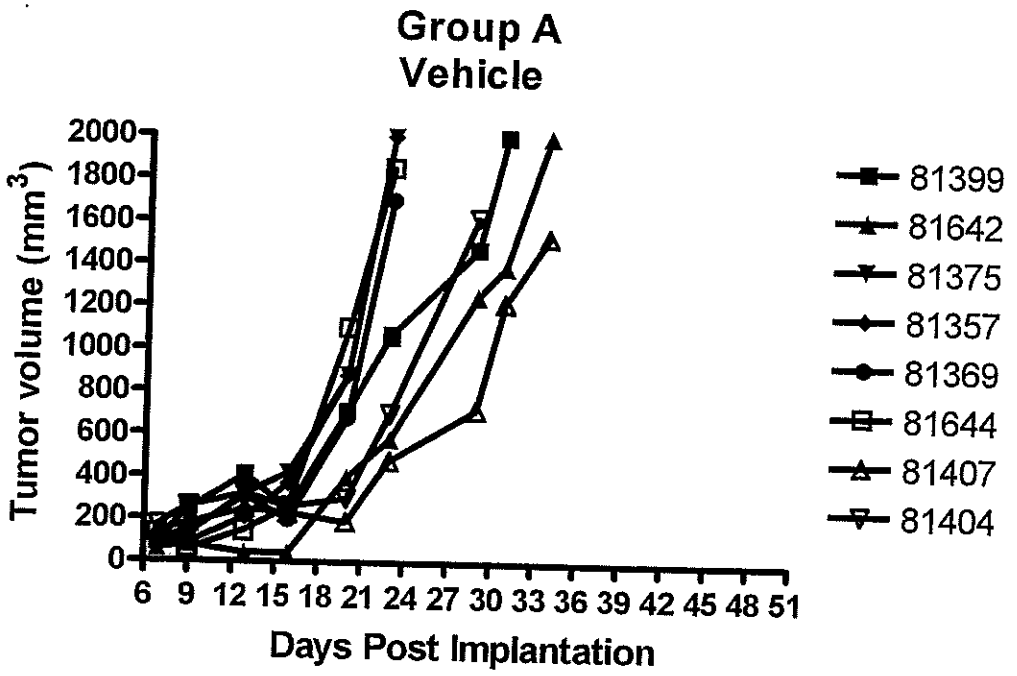


Figure 33A

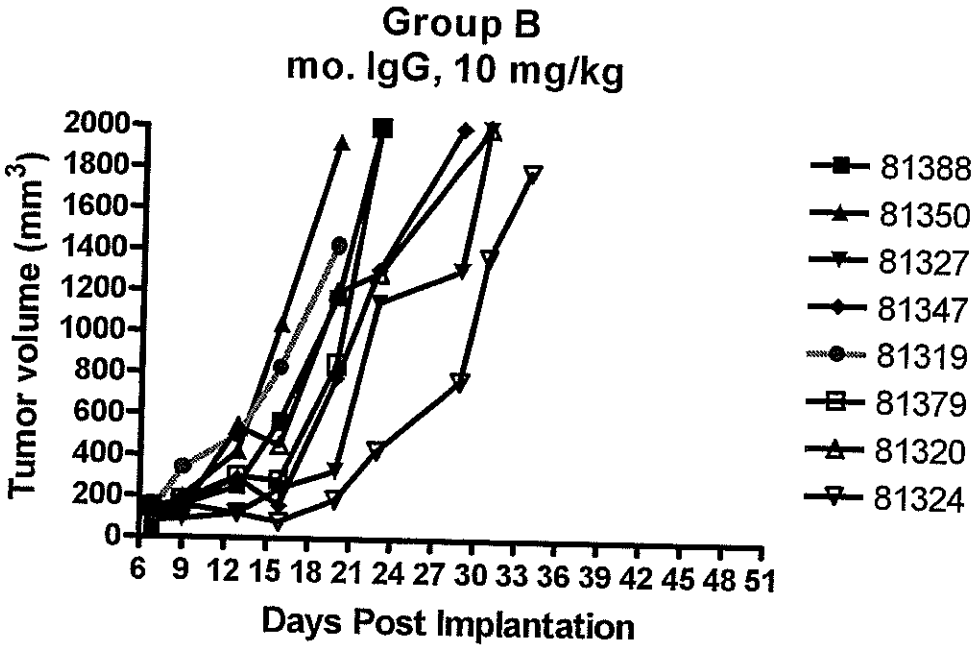


Figure 33B

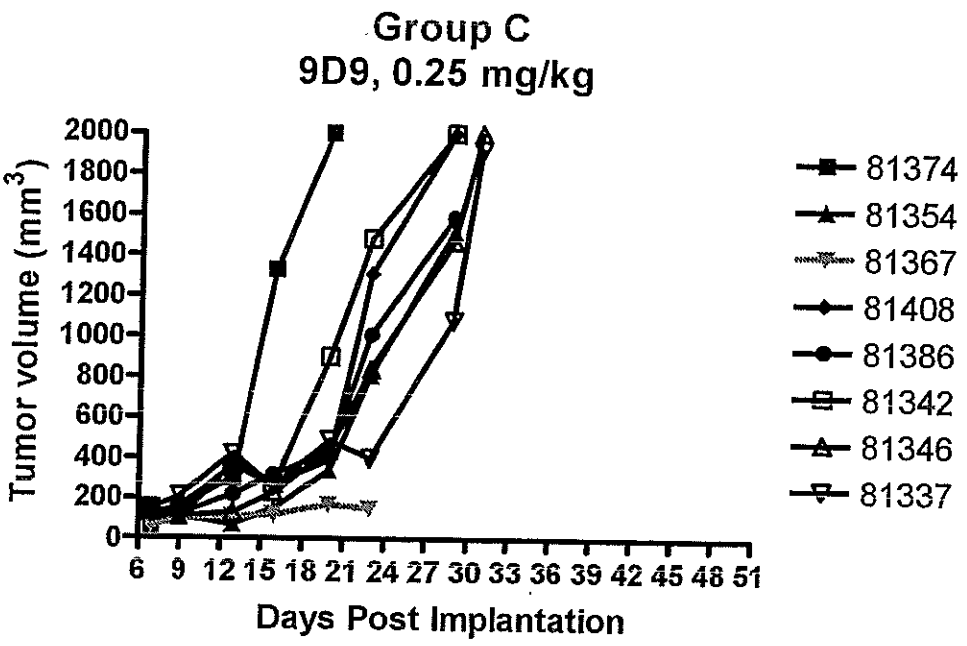


Figure 33C

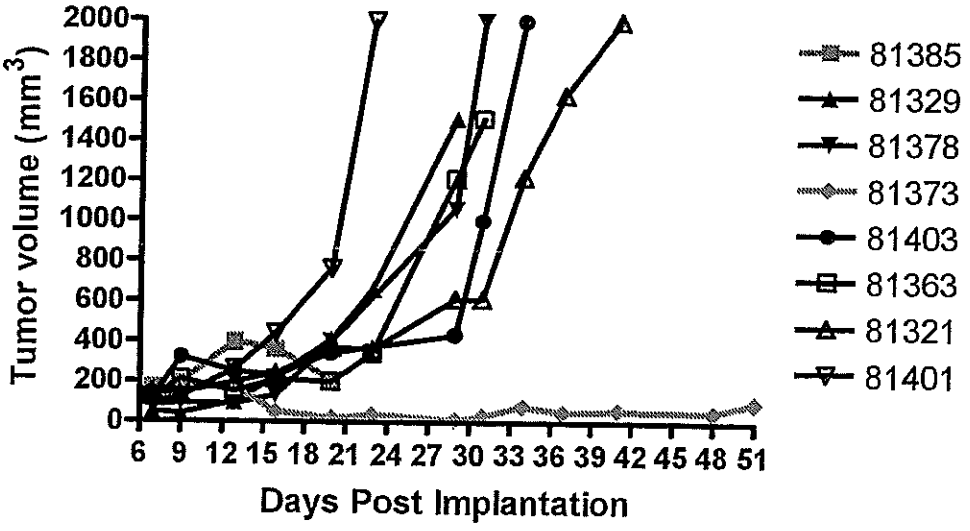


Figure 33D

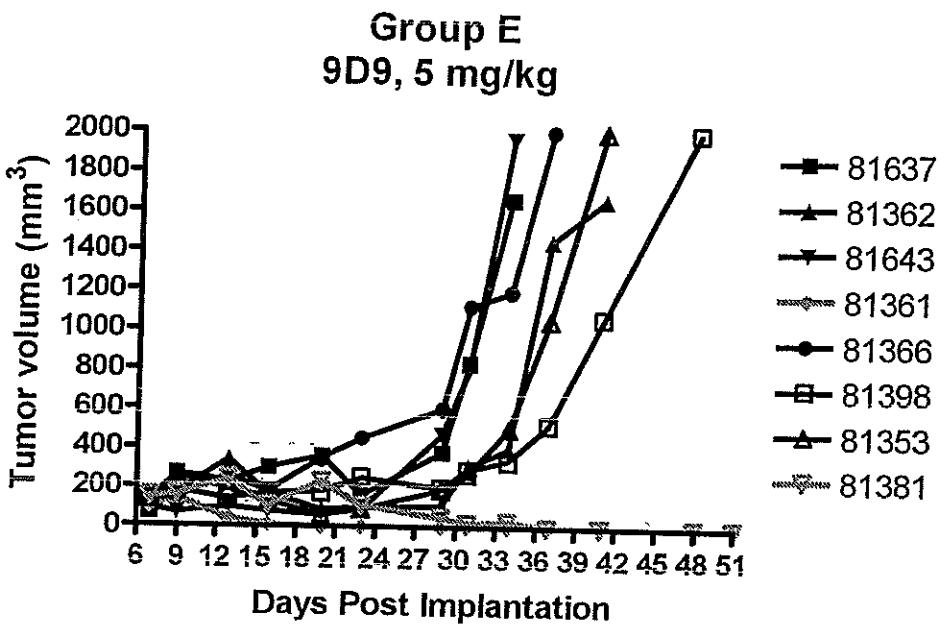


Figure 33E

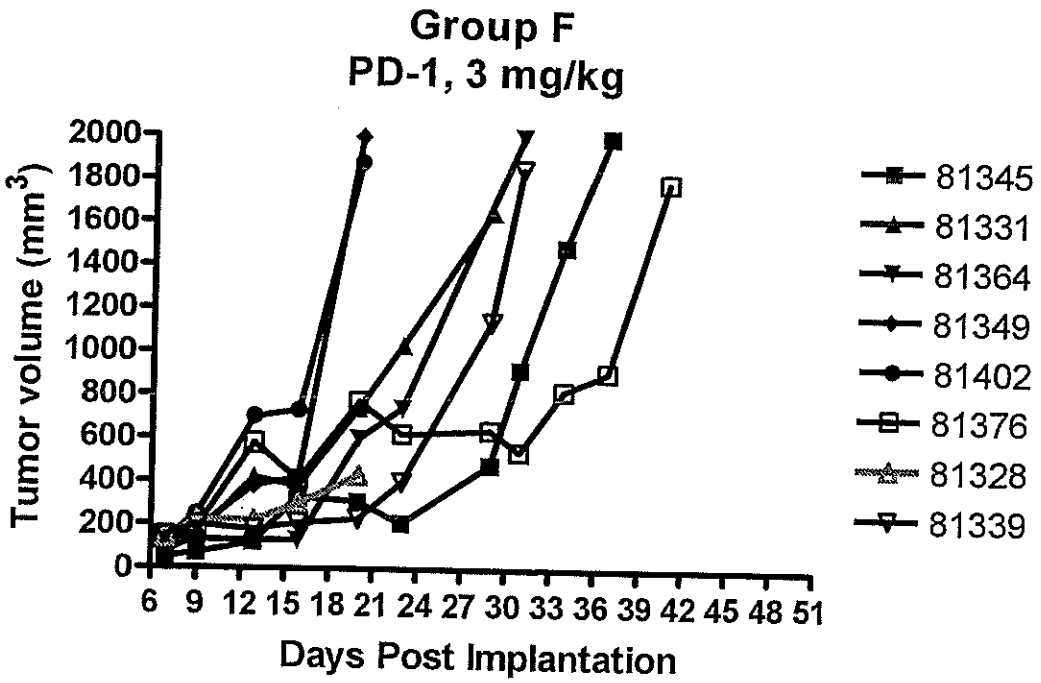


Figure 33F

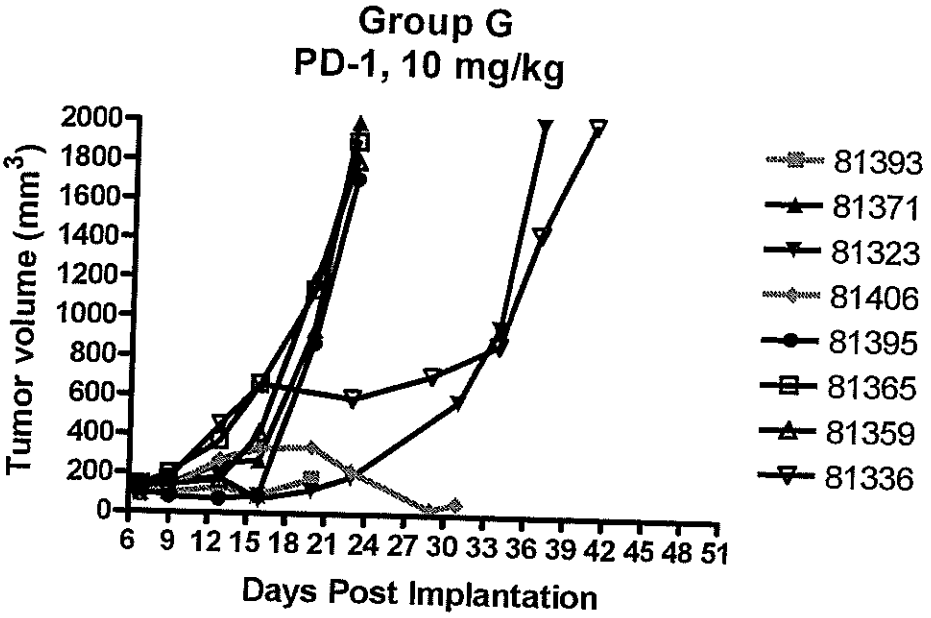


Figure 33G

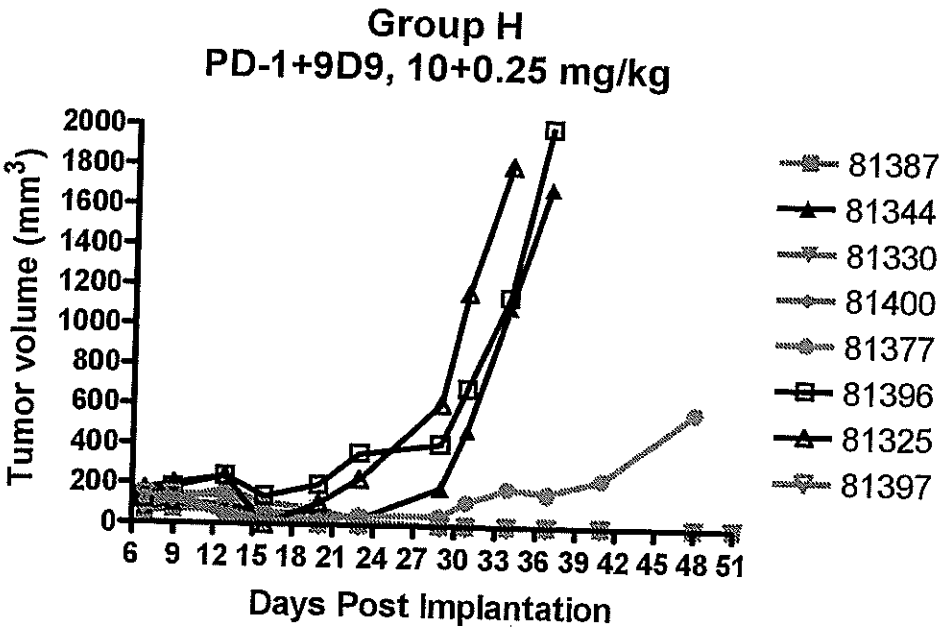


Figure 33H

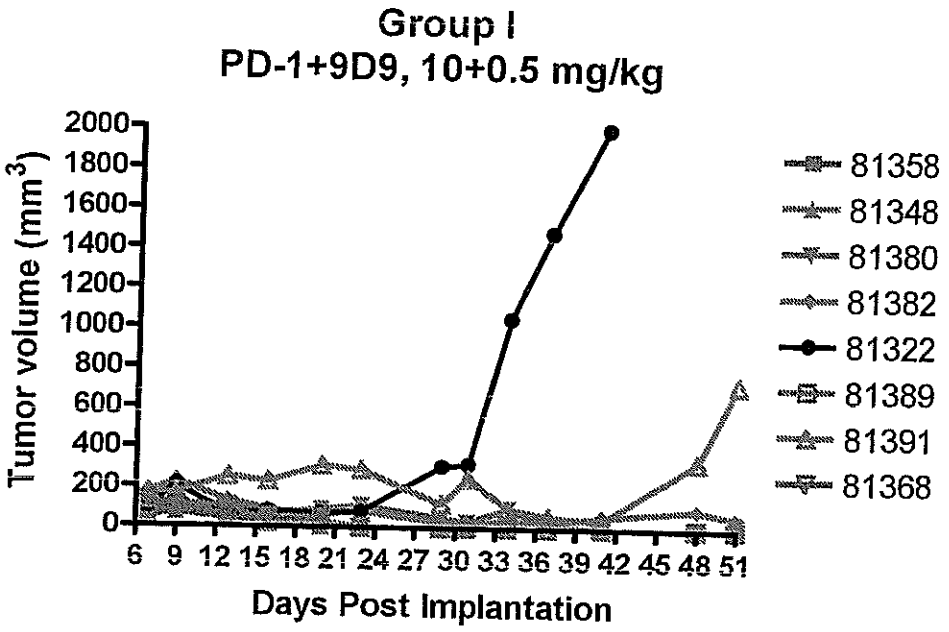


Figure 33I

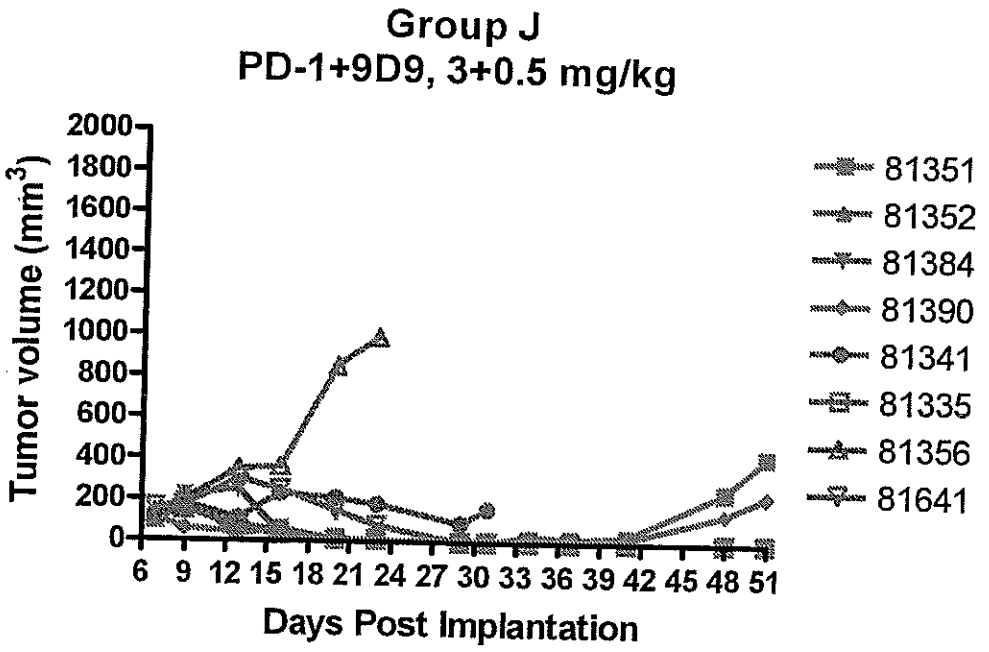


Figure 33J

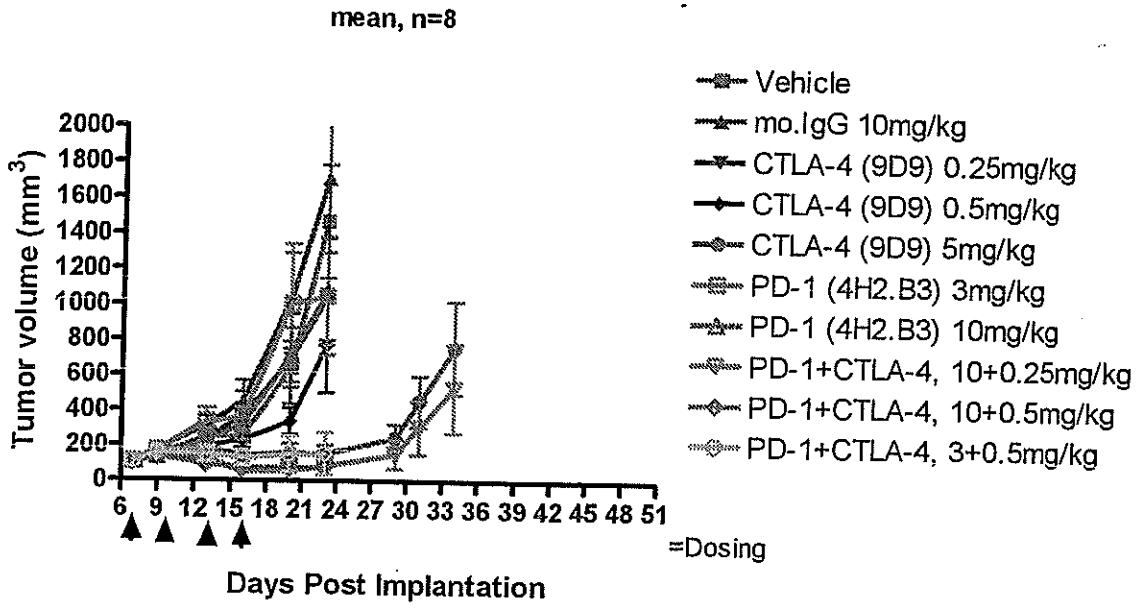


Figure 34

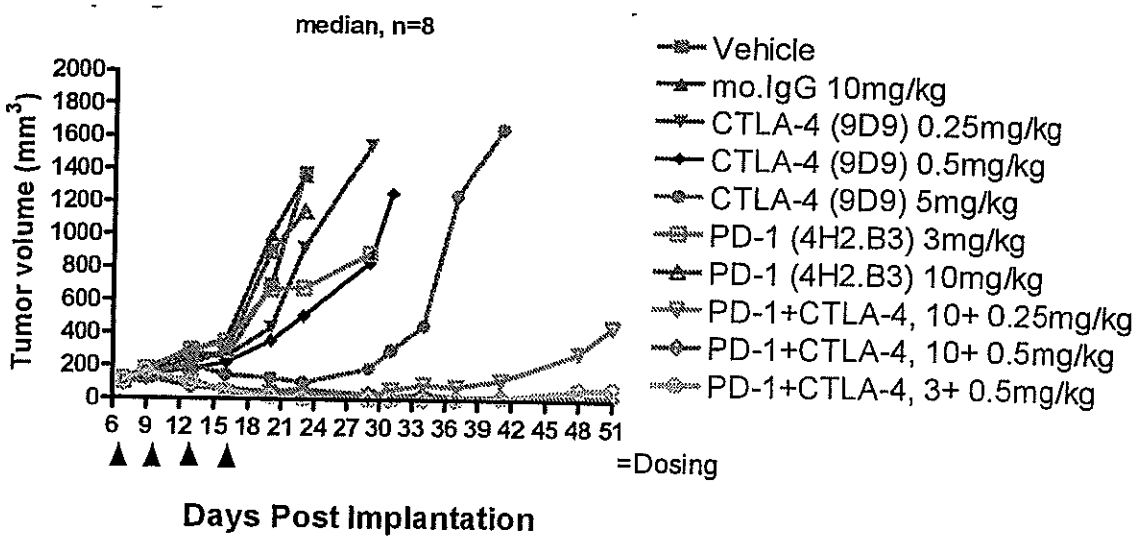


Figure 35

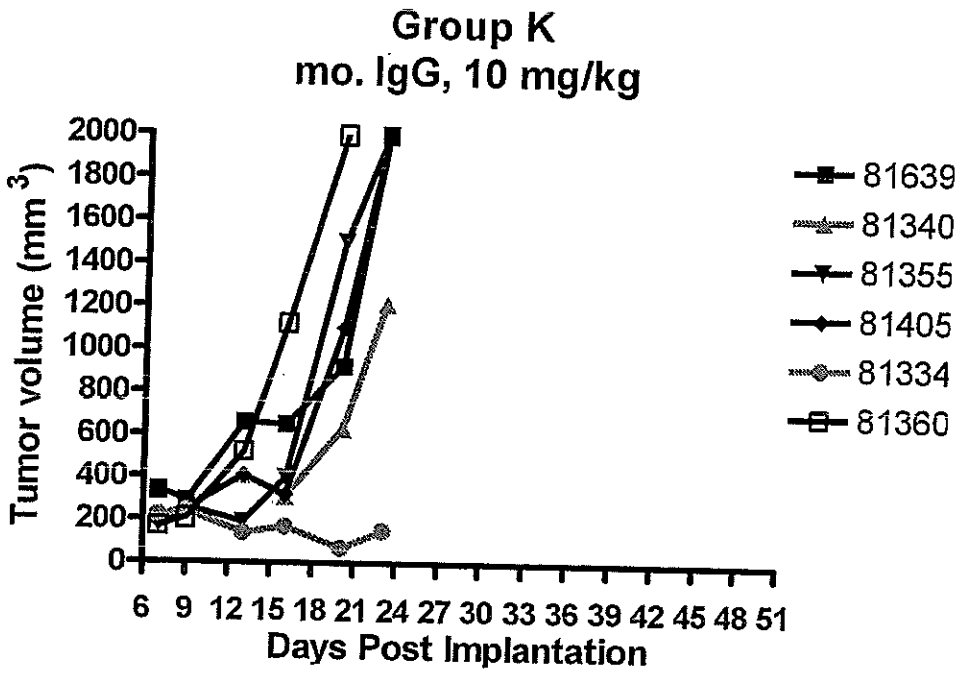


Figure 36A

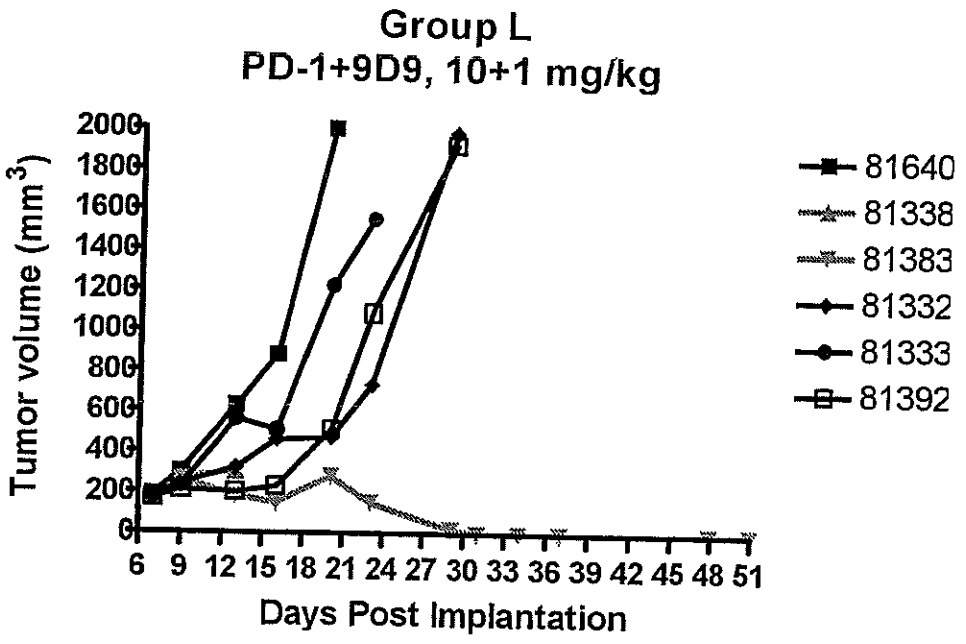


Figure 36B

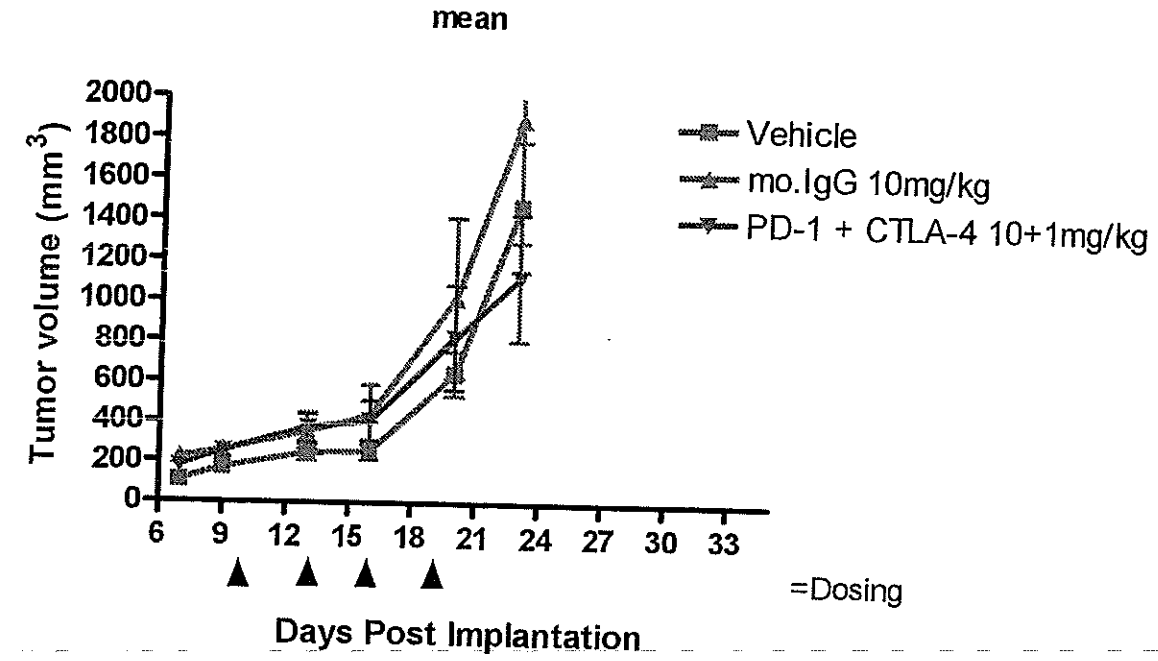


Figure 37

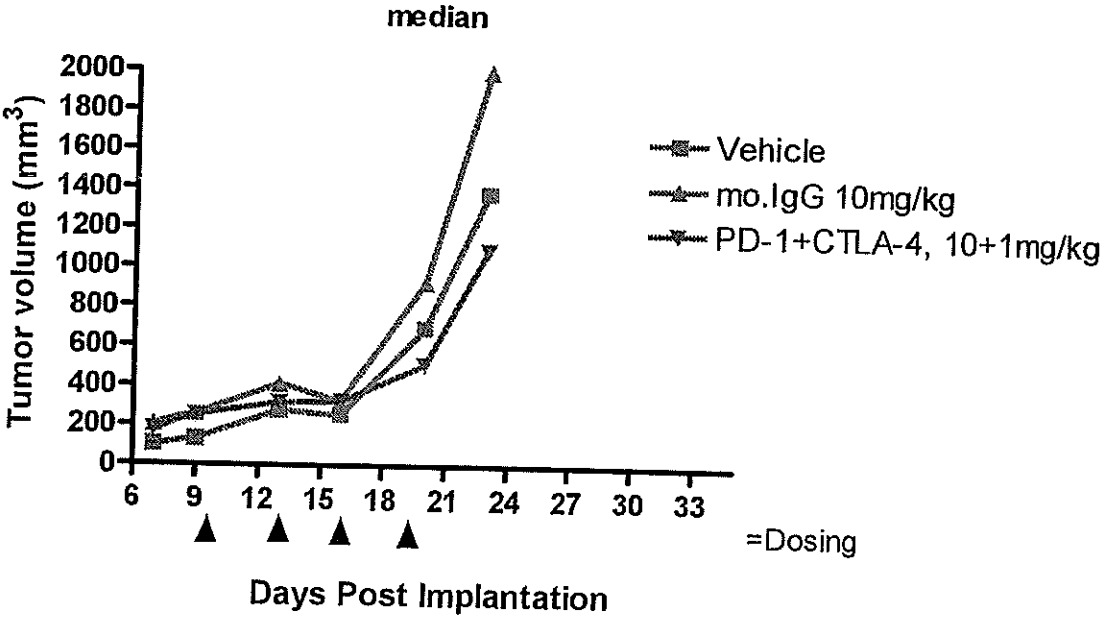


Figure 38

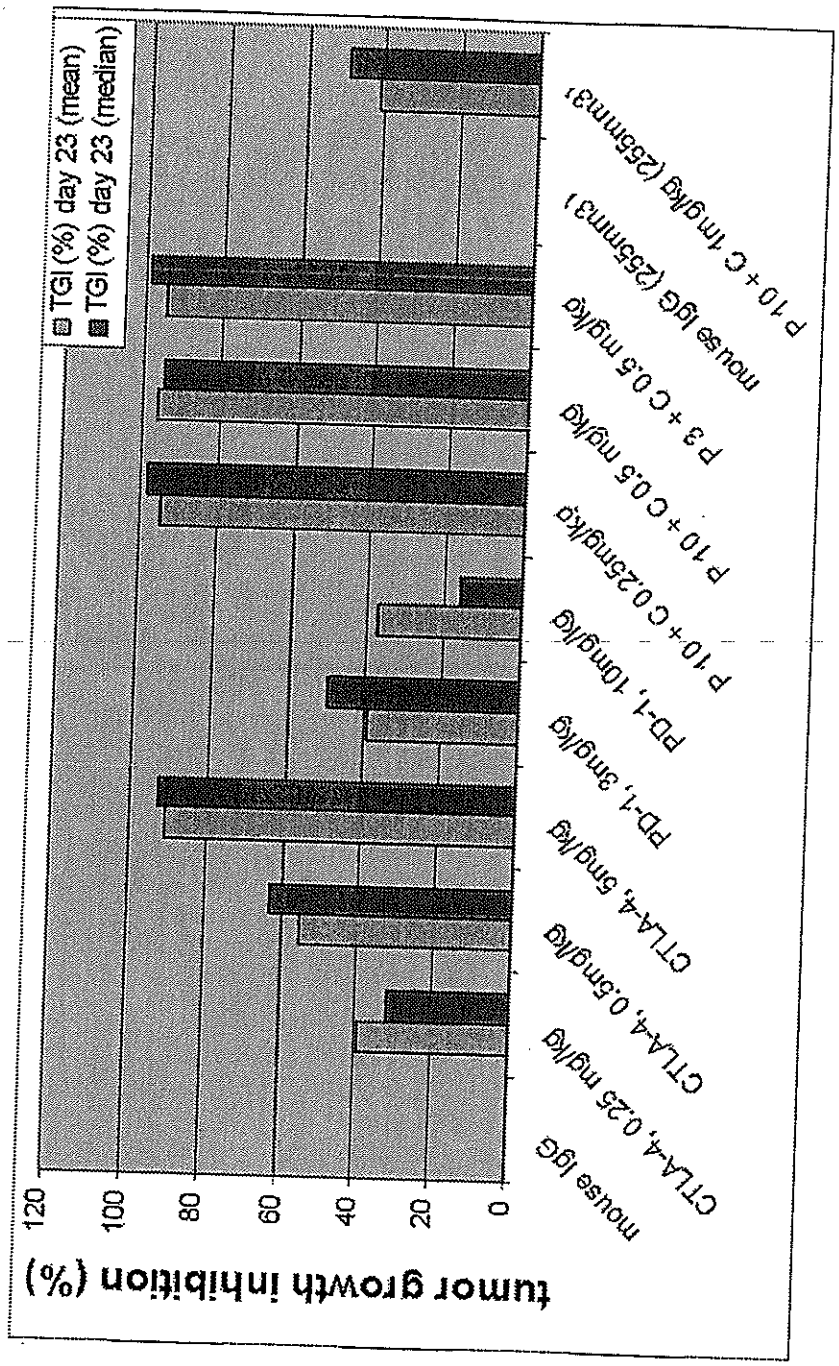

TGI (%) day 23 (mean)
TGI (%) day 23 (median)
tumor growth inhibition (%)
120
100
80
60
40
20
0
mouse IgG
CTLA-4, 0.25 mg/kg
CTLA-4, 0.5mg/kg
CTLA-4, 5mg/kg
PD-1, 3mg/kg
PD-1, 10mg/kg
P 10+C 0.25mg/kg
P 10+C 0.5 mg/kg
P 3 +C 0.5 mg/kg
mouse IgG (265mm3)
P 10 + C 1mg/kg (265mm3)

Figure 39

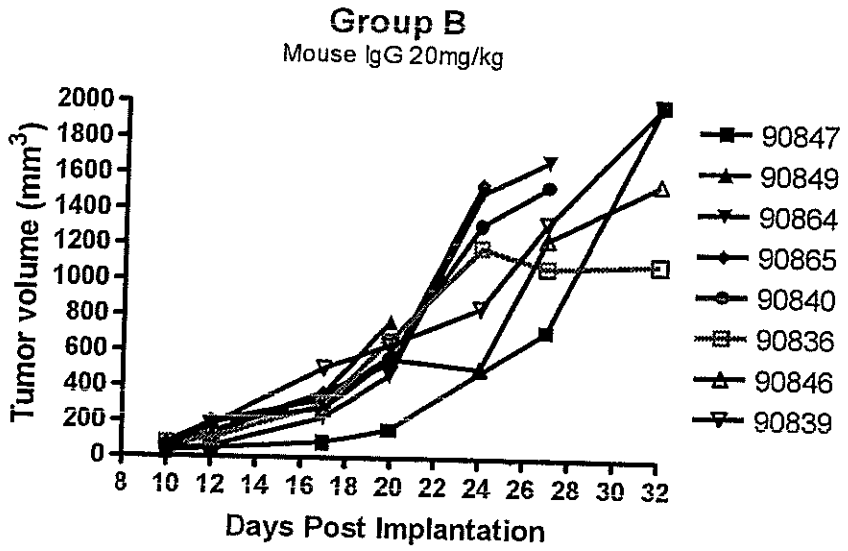


Figure 40A

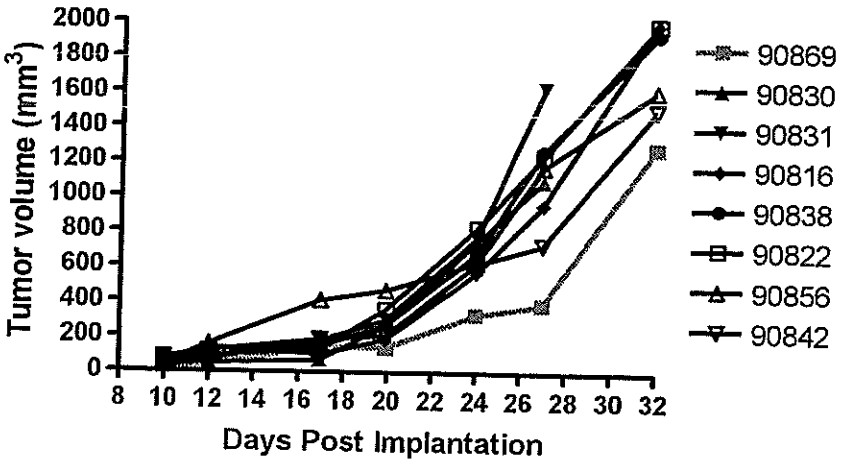


Figure 40B

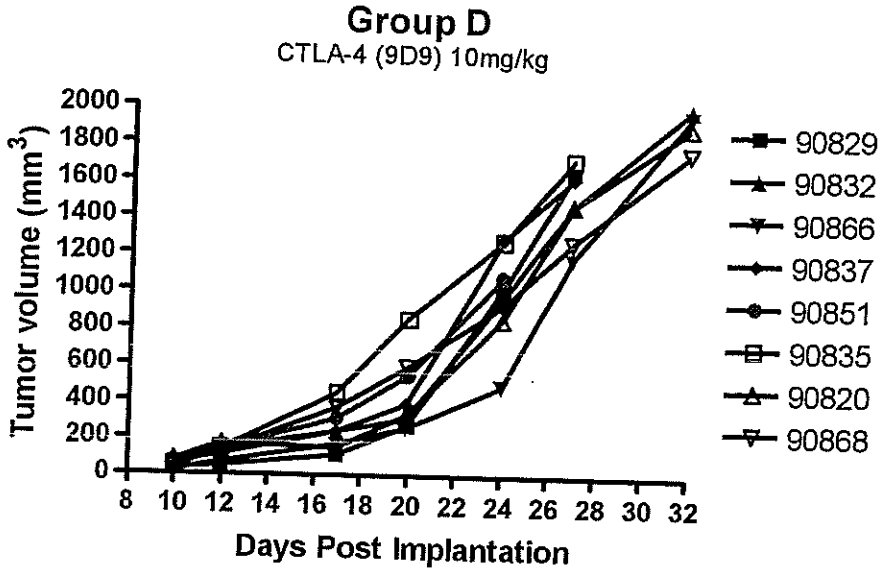


Figure 40C

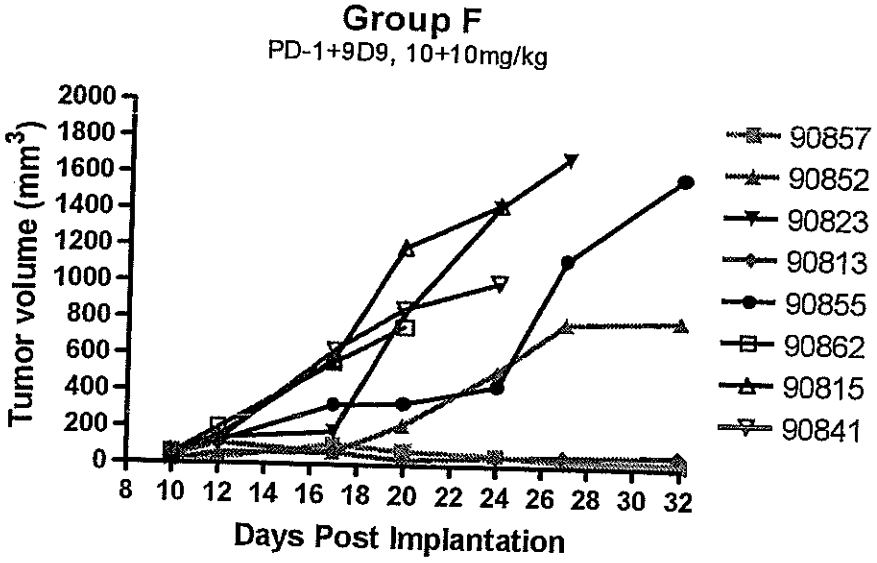


Figure 40D

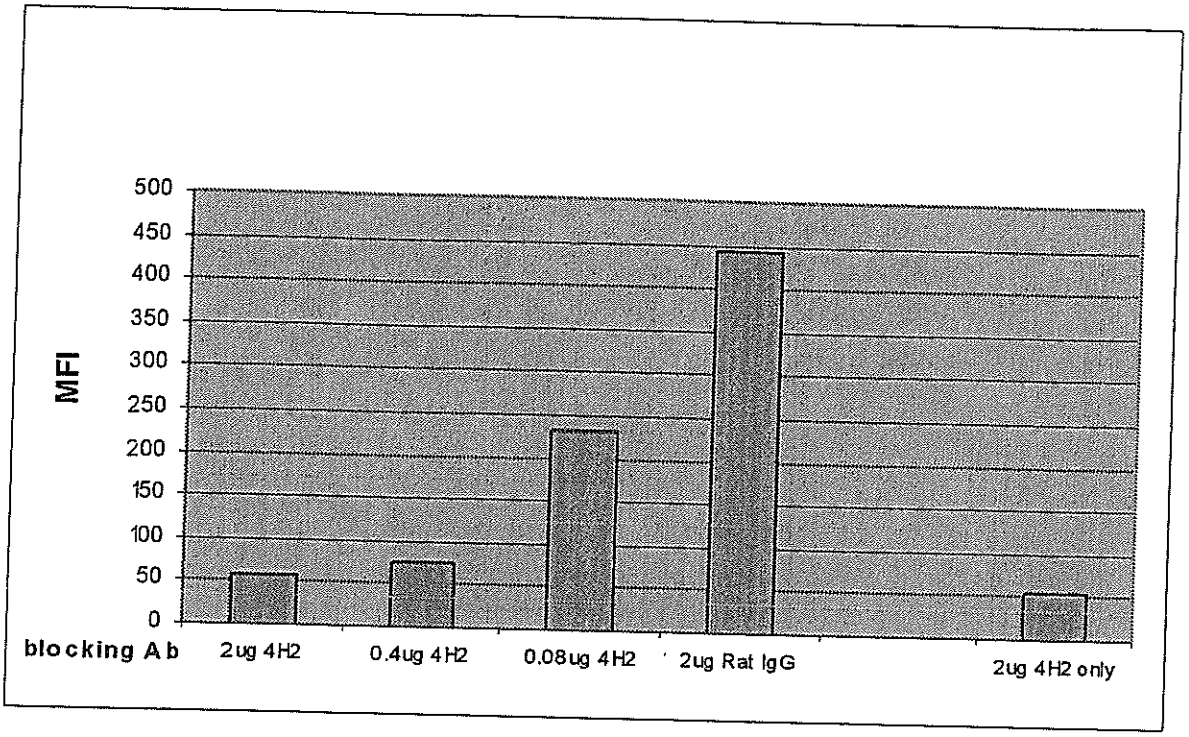


Figure 41

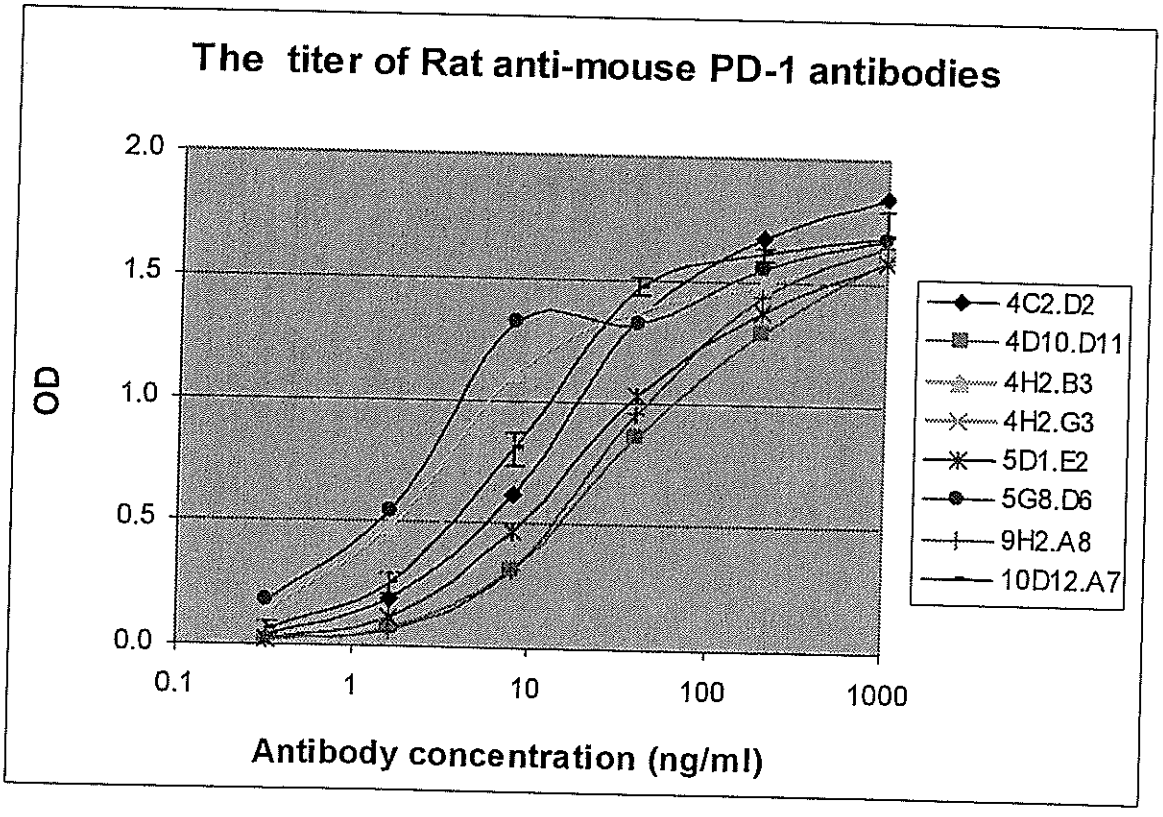


Figure 42

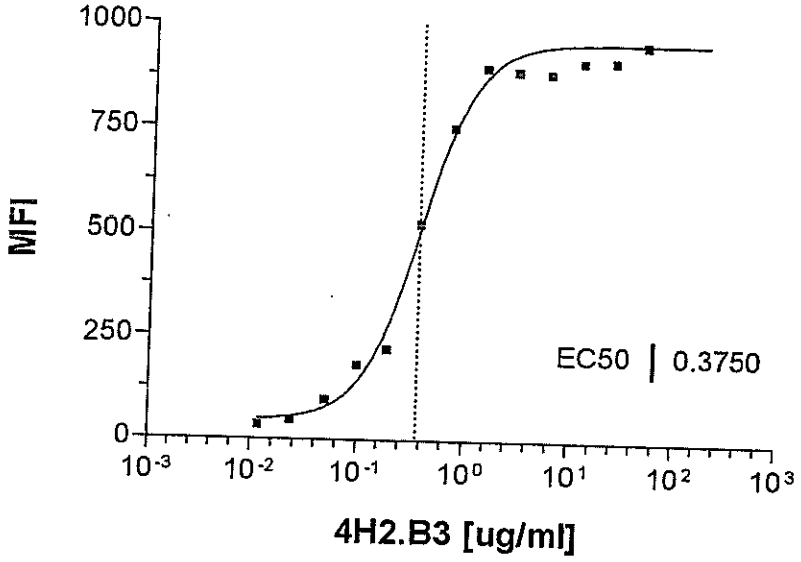


Figure 43

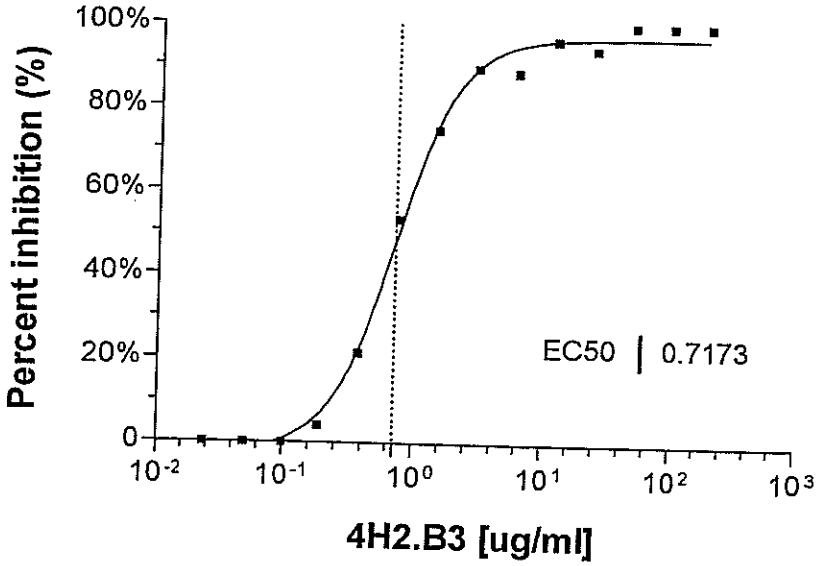


Figure 44

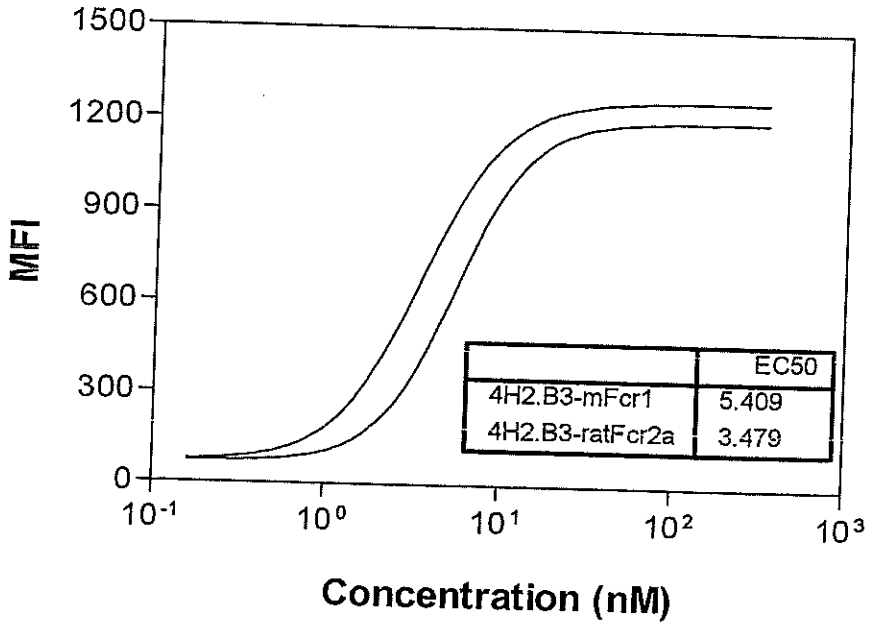


Figure 45

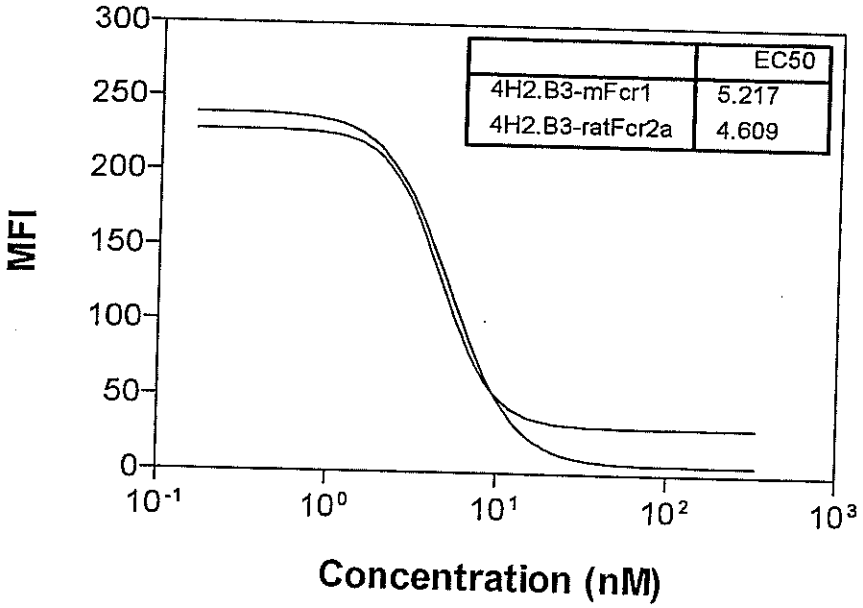


Figure 46

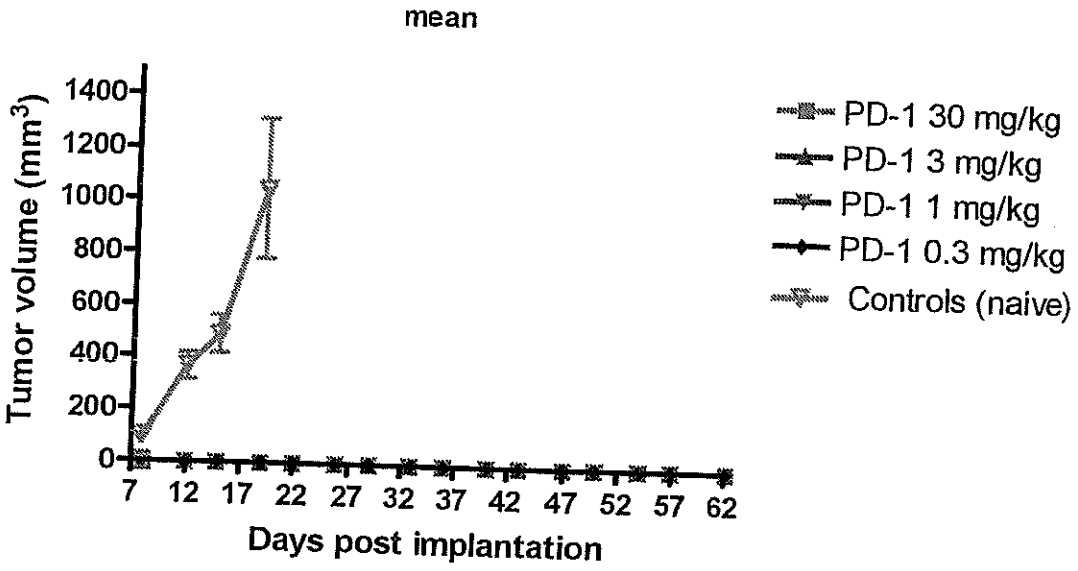


Figure 47

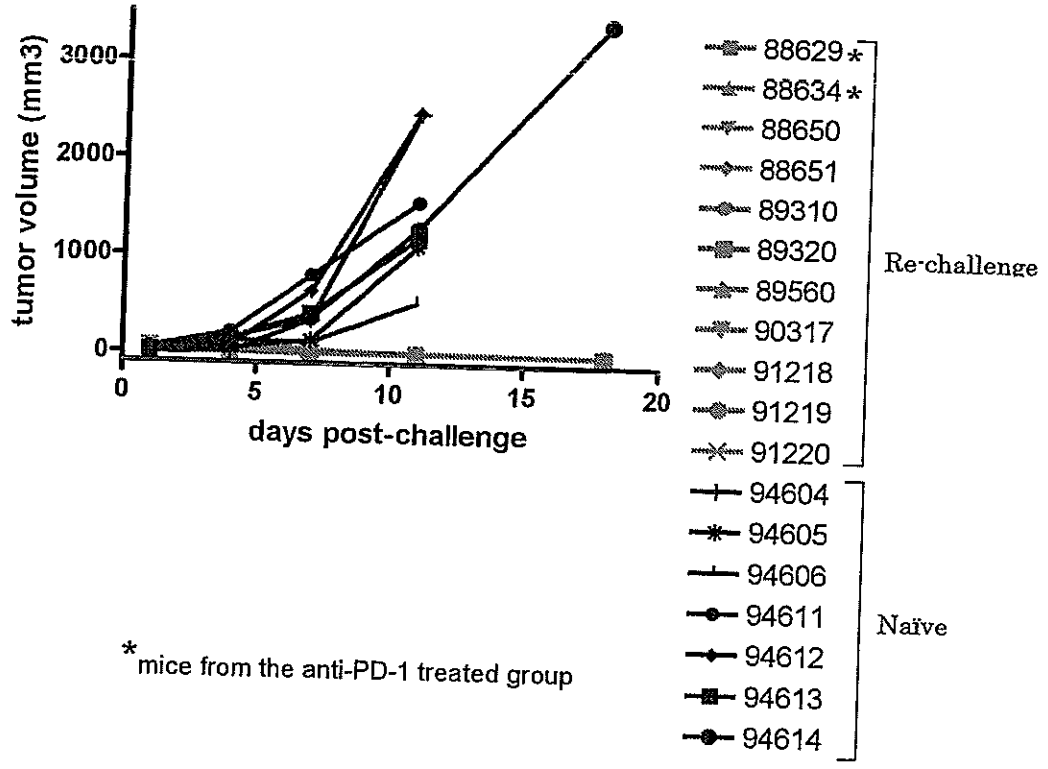


Figure 48

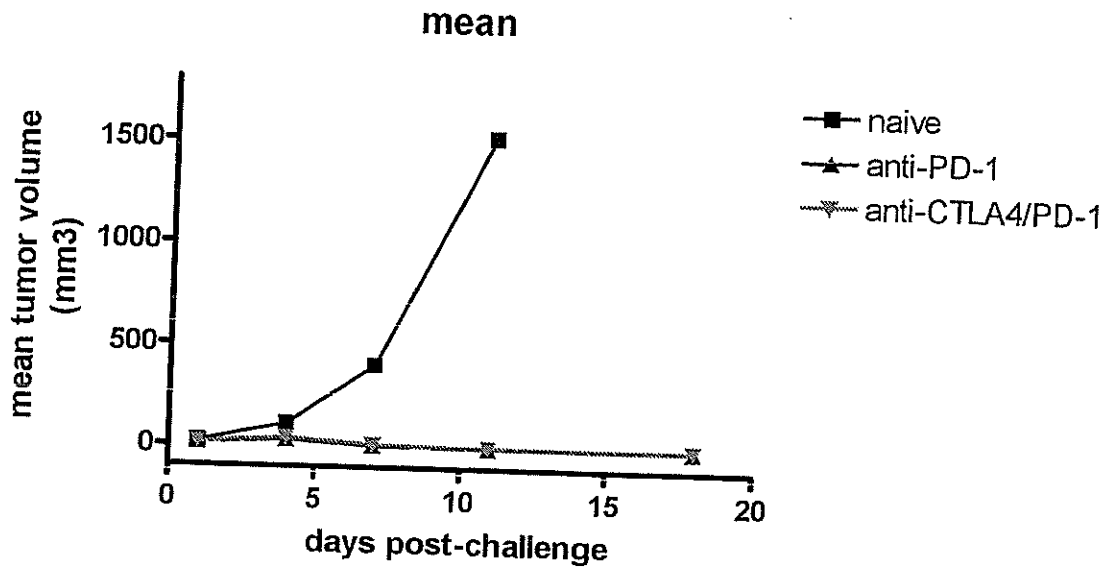


Figure 49

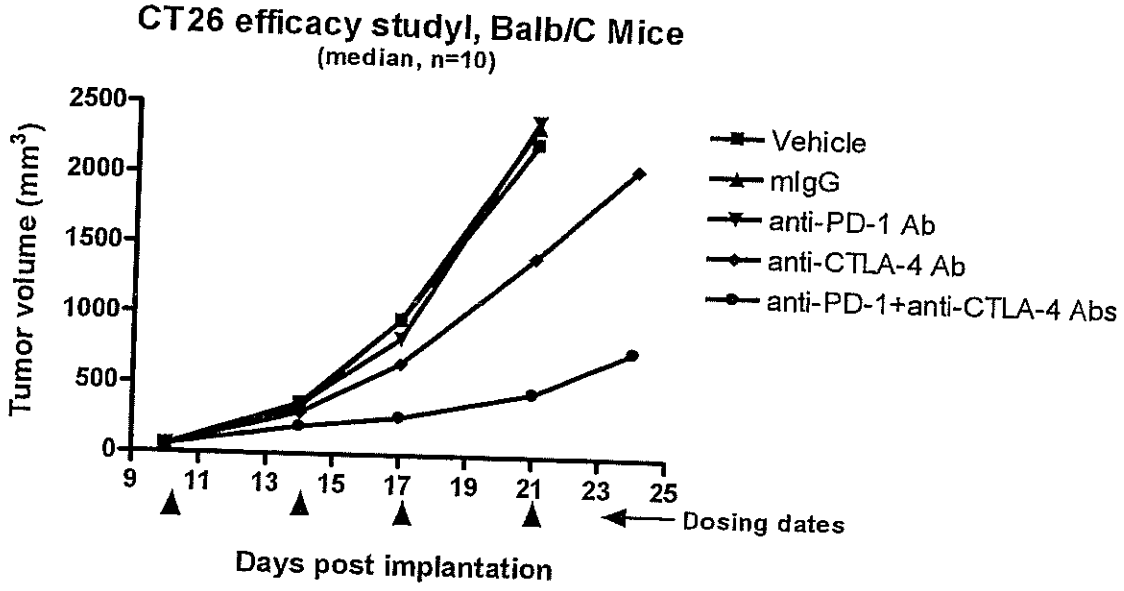


Figure 50

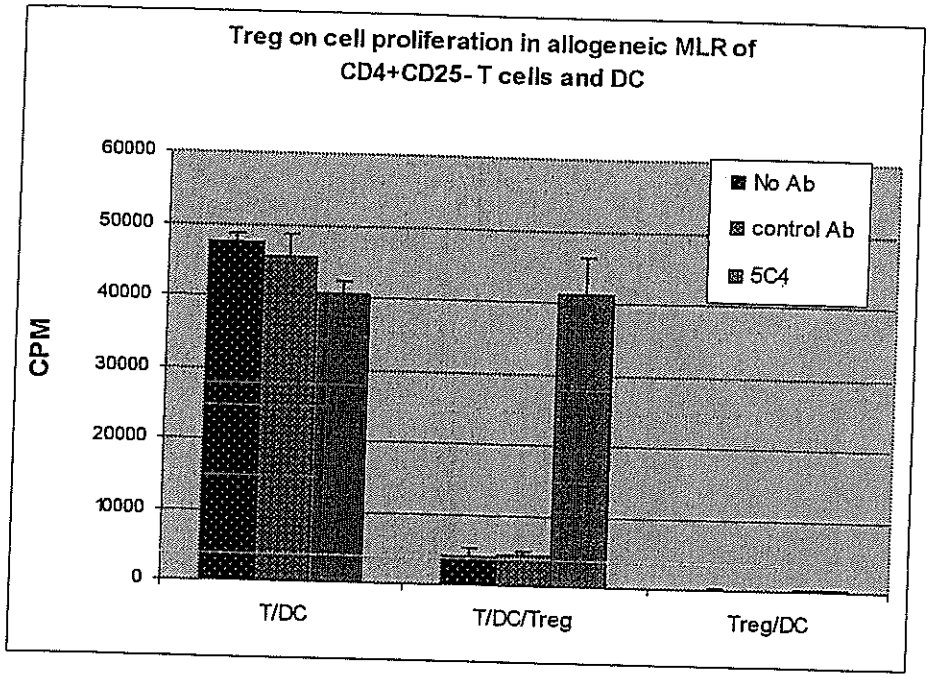


Figure 51A

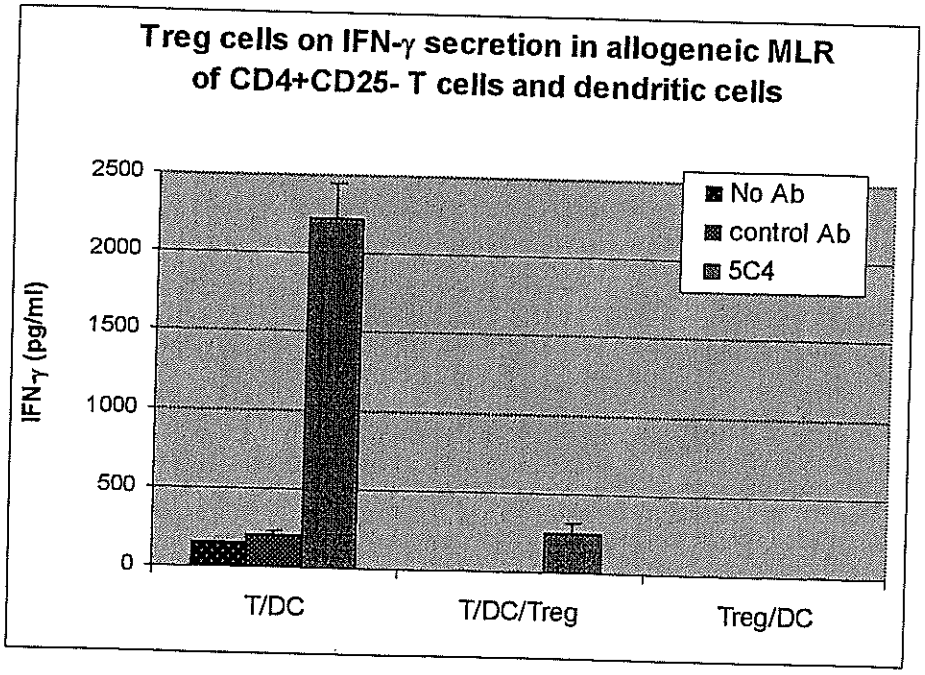


Figure 51B

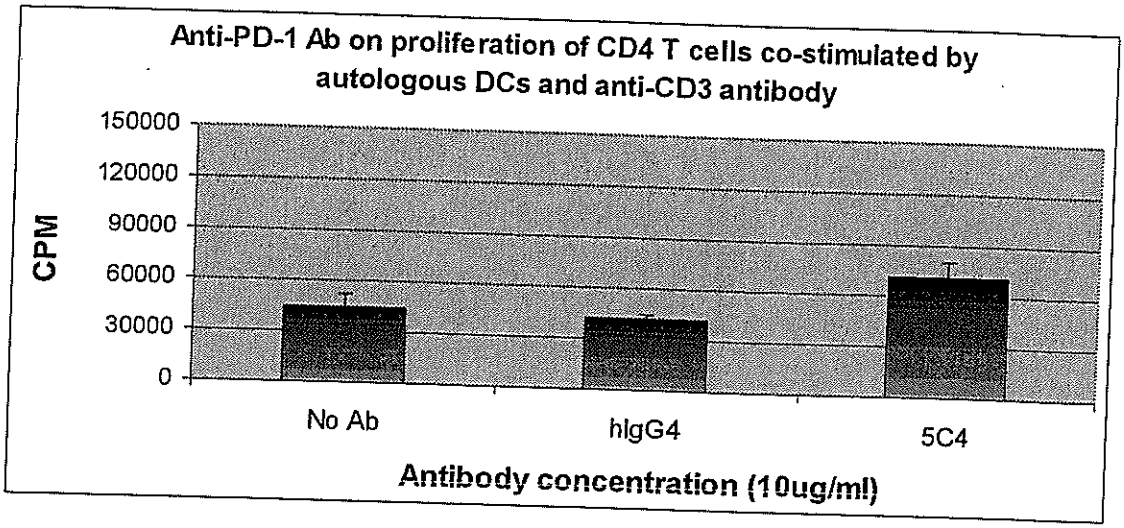


Figure 52A

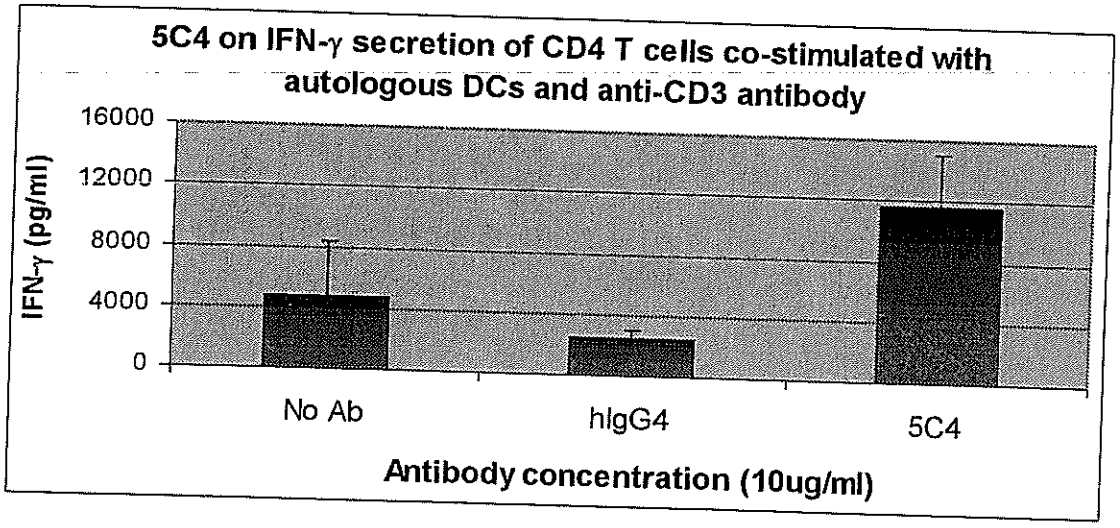


Figure 52B

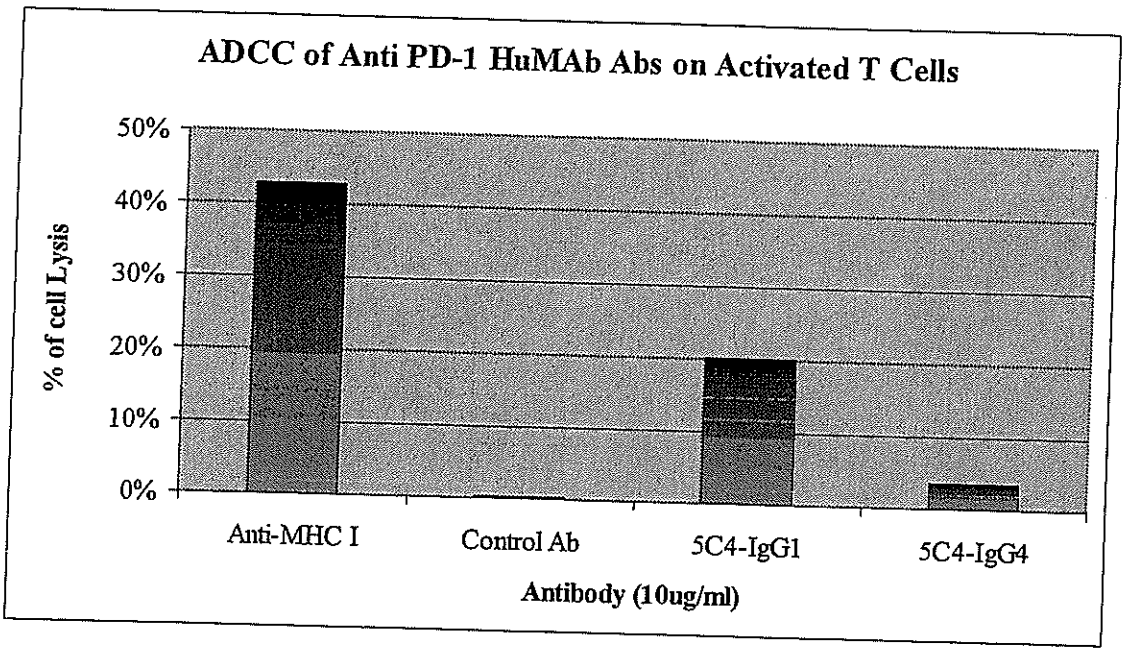


Figure 53

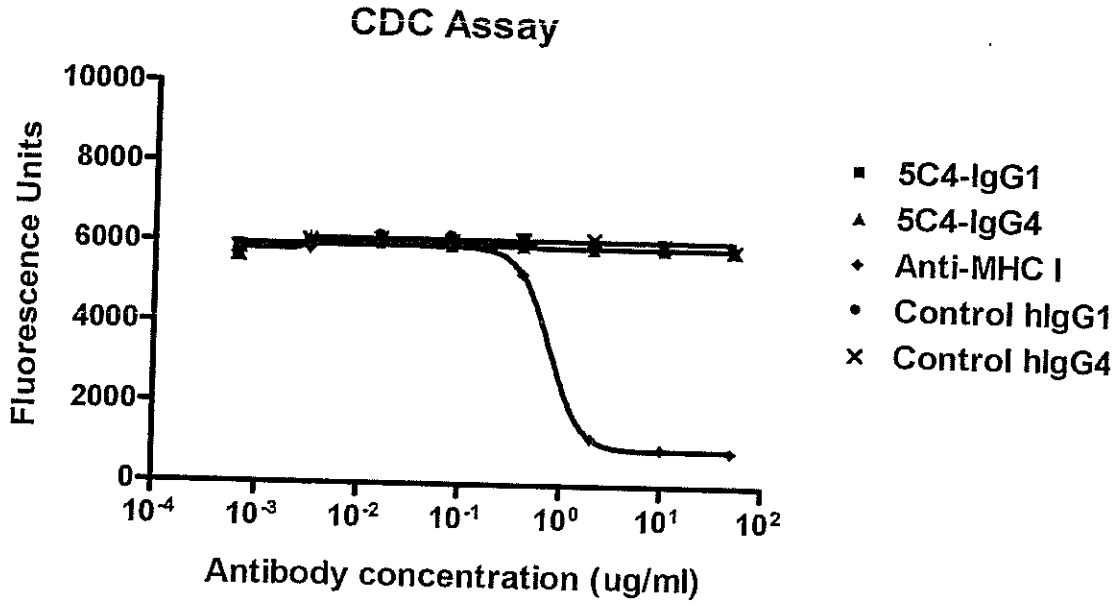


Figure 54